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## PNEUMONIA IN PRIVATE PRACTICE

A STUDY OF 911 CASES

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Much has been written in recent times concerning pneumonia especially as regards the incidence of the various types of pneumococcic pneumonia and their amenability to serum therapy. When compared, these reports have shown a rather striking consistency both in the incidence of pneumococcus types and in the results obtained with specific treatment. However, these studies have been based largely on material observed in large city hospitals such as Bellevue and Harlem hospitals in New York and the Boston City Hospital. So far as we know, there have been no modern studies published on pneumonia in private practice. The impression seems to be general, however, that the death rate for pneumonia in private practice is considerably lower than it is in large city hospitals. While in hospital wards the fatality rate may run from 30 to 35 per cent, one often hears practitioners assert that in private practice they rarely lose a patient with pneumonia, and Osler, quoting Howard and Fussell, states that the fatality rate in the latter group varies between 6 and 17 per cent.<sup>1</sup>

In the hope of throwing some additional light on this subject, we have collected 911 cases of pneumonia from private practice. The number of cases included is not as large as we should have liked it to be, but at least it is large enough to form a basis for certain general conclusions.

This study falls naturally into three divisions: (1) patients treated at home, (2) patients treated in the private pavilions of hospitals, and (3) patients seen in consultation in private practice.

### PATIENTS TREATED AT HOME

Our original intention was to collect the material for this study from all three of the sources mentioned. We found it almost impossible, however, to obtain adequate records on patients who had been treated in the home. Through the kindness of Dr. Edward S. Rogers, director of the New York State Bureau for Pneumonia Control, we are able to quote the following figures from his investigations in New York State: Rogers found that in 1,475 hospital cases of pneumococcus type I pneumonia the fatality rate was 18.5 per

cent, whereas in 551 cases of the same type in which treatment was given in the home the death rate was only 13.4 per cent, a difference of 5 per cent. All the patients in both series received type I serum. These patients were not citizens of New York City but were collected from cities, towns and rural districts in New York State excluding New York City.

The factors that may influence this difference in the fatality rate of patients treated in the hospital and those treated at home will be discussed later.

### PATIENTS FROM THE PRIVATE PAVILIONS OF HOSPITALS

The greater part of the material for this study (560 cases) was obtained from the private wards of New York City hospitals. These patients were all admitted during the last decade (1928-1938) and all had been "typed" by standard methods. Many cases of typical lobar pneumonia (more than 50 per cent) had to be excluded from our survey because of inadequate bacteriologic study. The hospitals whose records were used in the compilation were the Doctors' Hospital, Fifth Avenue Hospital, Mount Sinai Hospital, New York Hospital, Post-Graduate Hospital, Presbyterian Hospital and Saint Luke's Hospital, all in the city of New York.<sup>2</sup>

**Bacteriologic Classification.**—In table 1 it will be noted that approximately 95 per cent of the cases of pneumonia in this series are of pneumococcic origin. This agrees very closely with the observations of Cecil, Baldwin and Larsen<sup>3</sup> in their statistical study of 2,000 cases of pneumonia at Bellevue Hospital and with the results reported by the workers from Rockefeller Institute.<sup>4</sup> In all these studies, *Streptococcus haemolyticus* pneumonia ranks second in prevalence, averaging about 3 per cent of the total series.

**Age and Sex Distribution.**—The most important fact brought out in this connection was that the average age in this series of 560 pavilion patients was 45 years, whereas the average age in our Bellevue studies was only 38 years. The sexes were about equally represented, in contrast to studies made in city hospitals, in which the males have far outnumbered the females. In the present study 53.6 per cent were males and 46.4 per cent females. In the Bellevue Hospital studies 83.1 per cent were males and 16.9 per cent females.

**Incidence of the Various Types of Pneumococcic Pneumonia.**—Table 2 shows the incidence of the dominant types of pneumococcic pneumonia. Type III pneumonia was the most prevalent (20.2 per cent). In

2. The attending physicians at the hospitals mentioned gave us access to the records of private patients.

3. Cecil, R. L.; Baldwin, H. S., and Larsen, N. P.: Lobar Pneumonia, Arch. Int. Med. 40: 253-280 (Sept.) 1927.

4. Avery, O. T.; Chickering, H. T.; Cole, Rufus, and Dochez, A. R.: Acute Lobar Pneumonia, Monograph 7, Rockefeller Institute for Medical Research, Oct. 16, 1917.

From the Medical Department of the Cornell University Medical College.

1. Osler, Sir William: The Principles and Practice of Medicine, ed. 1, New York, D. Appleton & Co., 1910.



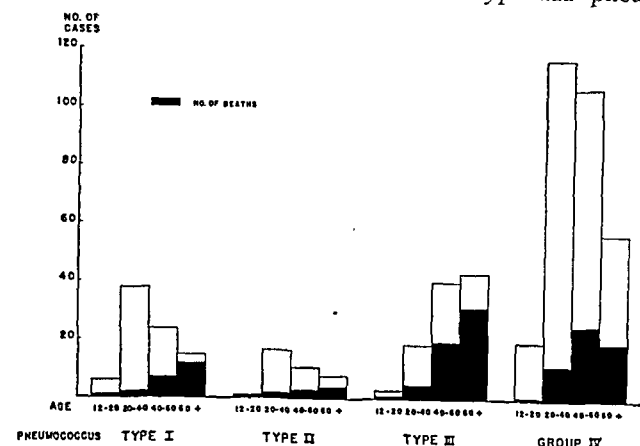
this respect the present series differs sharply from previous studies, in which type I has been the commonest type. This difference in type distribution can be explained at least in part by the higher age incidence of pneumonia in private patients. The studies by Cecil and his co-workers<sup>5</sup> at Bellevue Hospital showed clearly that the incidence of type III pneu-

the ages of 20 and 40; of type III, after the age of 60, in contrast to the Bellevue figures, which show that the highest incidence of type I occurred between the ages of 20 and 30, and of type III between 30 and 50.

**Clinical Characteristics.**—The various forms of pneumonia showed the characteristics that have been described in previous studies. Cases due to pneumococci of types I, II and III were nearly always typical lobar infections with classic history, frank physical signs and rusty sputum. The seriously ill patients usually showed signs of multilobar involvement. The "miscellaneous" types often presented an atypical picture, with only partial consolidation of the lobes and purulent rather than bloody or rusty sputum. The patients with streptococcal or staphylococcal infections were, almost without exception, seriously ill but with indefinite signs in the chest.

**Bacteremia.**—Unfortunately, blood cultures were not taken as a routine in this group of patients. However, 287 patients were subjected to blood cultures, and the results are shown in table 3.

Approximately 24 per cent of the patients in this series yielded positive blood cultures, and in the septic cases the fatality rate was 74 per cent. Patients with negative blood cultures showed a fatality rate of only



Incidence and fatality rates for pneumococcus types in relation to age (private pavilion series).

monia increases with age, an observation which has been corroborated by Blake<sup>6</sup> and others.

In table 2 one also notes a very high incidence of the miscellaneous types (57.3 per cent), much higher than in most of the series reported from other institutions. Whether this was actually the case or whether the typing was inaccurate it is impossible to say. The newer types have not been separately listed in table 2, as they were recognized only during the last few years of the period covered by the study.

TABLE 1.—Bacteriologic Classification of 560 Cases of Pneumonia from Private Pavilions

Bacteria	Number of Cases	Incidence, per Cent
<i>Pneumococcus</i> (all types).....	531	94.8
<i>Streptococcus haemolyticus</i> .....	19	3.4
<i>Streptococcus viridans</i> .....	2	0.35
<i>Bacillus influenzae</i> .....	1	0.2
<i>Staphylococcus aureus</i> .....	4	0.7
<i>Staphylococcus albus</i> .....	1	0.2
<i>Friedländer's bacillus</i> .....	2	0.35
Total.....	560	100.00

TABLE 2.—Incidence of *Pneumococcus* Types in Private Pavilion Series

Type of <i>Pneumococcus</i>	Cases	Incidence, per Cent
<i>Pneumococcus</i> type I.....	83	15.6
<i>Pneumococcus</i> type II.....	37	6.9
<i>Pneumococcus</i> type III.....	107	20.2
Miscellaneous types (group IV).....	304	57.3
Total.....	531	100.0

It is noteworthy that 78.4 per cent of the cases of type II pneumonia occurred in the male and only 21.6 per cent in the female.

In 531 cases of pneumococcal pneumonia in private pavilions, the incidence of type I was highest between

5. Cecil, R. L.; Plummer, Norman, and McCall, Marsh: *Pneumococcus Type III Pneumonia*, Am. J. M. Sc. 191: 305 (March) 1936.  
6. Blake, F. G.: Observations on *Pneumococcus* Type III Pneumonia, Ann. Int. Med. 5: 673-686 (Dec.) 1931.

TABLE 3.—Blood Cultures in the *Pneumococcus* Series

Type of <i>Pneumococcus</i>	Positive Blood Cultures		Negative Blood Cultures	
	Number	Fatality, per Cent	Number	Fatality, per Cent
Type I.....	12	8	35	5
Type II.....	4	3	19	1
Type III.....	26	21	47	20
Miscellaneous types	27	19	114	9
Total.....	69	51	218	35

16 per cent. However, the figure was unusually high (42.6 per cent) for forty-seven patients with type III pneumonia with sterile blood cultures.

**Complications.**—Analysis of the complications encountered in the series reveals nothing especially noteworthy. Empyema was the most prevalent complication, showing an incidence of 5 per cent in the pneumococcus series and 26.3 per cent in the cases of streptococcal pneumonia. Type I pneumonia showed an empyema incidence rate of 8.7 per cent. Endocarditis, meningitis and pericarditis were rarely reported. Fibrillation developed in quite a number of the older patients and was usually followed by a fatal termination.

**Fatality Rates.**—We were particularly interested in determining the fatality rate for patients in the private pavilions. Figures for the various types of pneumonia are recorded in table 4. Cases in which specific therapy was given are omitted. The death rate for pneumococcal pneumonia without serum therapy was 30.1 per cent, a figure which is generally looked on as about the standard for type I pneumonia without serum therapy. For example, Heffron's<sup>7</sup> figures on 2,047 cases of type I pneumonia in the United States and Canada in which serum therapy was not given showed a fatality rate of 30 per cent.

The fatality rate for *Streptococcus haemolyticus* pneumonia (47.4 per cent) approximates closely previous figures in the literature.<sup>8</sup>

7. Heffron, Roderick: Final Report of the Massachusetts Pneumonia Study and Service 1931-1935, Commonwealth 24, January-February-March 1937.

8. Bullowa, J. G. M.: Management of the Pneumonias, New York, Oxford Medical Publications, 1937.

The fatality rate for the entire group of 450 cases is 31.7 per cent, which checks pretty closely with the fatality rates for the wards of large city hospitals.

*Fatality Rates for Various Pneumococcus Types.*—The fatality rates for the dominant types of pneumococcic pneumonia are indicated in table 5 and are compared with similar figures from the series previously

TABLE 4.—Fatality Rates in Relation to Bacterial Etiology

Bacteria	Number of Cases	Deaths	Fatality, per Cent
<i>Pneumococcus</i> (no serum).....	421	127	30.1
<i>Streptococcus haemolyticus</i> .....	19	9	47.4
<i>Streptococcus viridans</i> .....	2	1	50.0
<i>Bacillus influenza</i> .....	1	0	0.0
<i>Staphylococcus aureus</i> .....	4	4	100.0
<i>Staphylococcus albus</i> .....	1	1	100.0
<i>Friedländer bacillus</i> .....	2	1	50.0
Total.....	450	142	31.7

TABLE 5.—Comparison of Fatality Rates Between Private Pavilion Series and Bellevue Hospital Series

Types of Pneumococcus	Present Series (No Serum)			Bellevue Hospital (No Serum)		
	No. of Cases	Deaths	Mortality, per Cent	No. of Cases	Deaths	Mortality, per Cent
Type I.....	31	10	32.0	234	73	31.2
Type II.....	23	7	30.4	441	215	48.8
Type III.....	102	56	54.9	500	210	42.0
Miscellaneous	265	54	20.4	373	109	29.2
Total.....	421	127	30.1	1,548	607	39.2

reported by one of us from Bellevue Hospital.<sup>3</sup> The fatality rates for pneumonia at Bellevue Hospital are proverbially high, but it will be seen from table 5 that the rates for our private pavilion series are not so far below them. Indeed, the fatality rate for 102 cases of type III pneumonia in the private pavilion series is considerably higher than that for a similar series at Bellevue.

As in all previous studies, the fatality rate for the various types increases with the age of the patient, as shown in the accompanying chart.

*Results with Serum Therapy.*—It is interesting to note that in only 60 per cent of type I cases in the private pavilion series was type I serum given. In the type II cases an even smaller proportion was given the benefit of specific therapy. In the newer types it was not to be expected that a high proportion of the patients would receive serum therapy because of the difficulty in many instances of obtaining the serum. However, in view of the well established efficacy of type I serum, it is difficult to understand why so many physicians withheld serum therapy from their type I cases.

Furthermore, the results obtained in fifty-two cases of type I pneumonia in which serum therapy was given were not so favorable as those which have been reported by various observers from large city hospitals such as Bellevue, Harlem<sup>9</sup> and the Boston City Hospital.<sup>9</sup> The reason for the high figure in the present series is easily discovered: In too many cases the serum treatment was initiated quite late in the disease.

Thirty-five patients with type I pneumonia were treated with serum during the first three days of the disease. In this selected group the fatality rate was only 14.3 per cent. In twelve cases of type II pneu-

monia in which serum therapy was instituted during the first three days there was only one death (8.3 per cent).

It must also be remembered that the average age in this series of patients is almost a decade higher than that reported in studies from various city hospitals. This factor must certainly be considered in comparing the results of serum in the present study with the results obtained elsewhere.

The value of serum therapy for the newer types, especially types V, VII and VIII, has been pretty well established by Bullowa,<sup>10</sup> Finland and Tilghman<sup>11</sup> and others. The results of serum treatment for the new types are well summarized by Lord and Heffron<sup>12</sup> in their recently revised monograph on pneumonia and serum therapy. In the present study the results with serum therapy in these types (table 6) were certainly encouraging, though the number of patients treated was too small to have much significance.

A few of the patients in this series received anti-pneumococcus rabbit serum. The number of patients, however, was not large enough to justify any inferences concerning its relative value as compared with horse serum. It is interesting to compare the total of 107 cases of all types in which serum was given with 221 cases in which none was given. The fatality rate in the group in which serum was given was approximately half of that for the group in which no serum was given (20.5 per cent versus 38.4 per cent).

PATIENTS SEEN IN CONSULTATION

In addition to the 560 cases studied in the private pavilions of hospitals, we have collected from our personal records 351 cases of pneumonia which were seen

TABLE 6.—Results of Serum Therapy in 107 Cases of Pneumonia from Private Pavilion Series

Types of Pneumococcus	Treated with Serum			Untreated		
	No. of Cases	Deaths	Mortality, per Cent	No. of Cases	Deaths	Mortality, per Cent
Type I.....	32	12	23.1	31	10	32.0
Type II.....	14	3	21.4	23	7	30.4
Type III.....	5	2	40.0	102	56	54.9
Type IV.....	6	2	33.3	11	0	0.0
Type V.....	6	1	16.7	7	3	42.9
Type VII.....	4	0	0.0	12	1	8.3
Type VIII.....	16	1	6.2	12	2	16.7
Type XIV.....	2	0	0.0	8	3	37.5
Type XV.....	0	0	0.0	7	1	14.3
Type XVIII.....	1	1	100.0	3	0	0.0
Type XIX.....	1	0	0.0	5	2	40.0
Total.....	107	22	20.5	221	85	38.4

TABLE 7.—Varieties of Pneumonia in Consultation Practice

Organism	No. of Cases	Incidence, per Cent	Deaths	Fatality, per Cent
<i>Pneumococcus</i> (all types).....	320	91.1	126	39.4
"	20	5.7	10	50.0
"	9	2.6	9	100.0
"	2	0.6	2	100.0
Total.....	351		147	41.9

only in consultation. The data obtained in these cases are naturally not as complete as those derived from the hospital charts of the private pavilion patients.

9. Sutliff, W. D., and Finland, Maxwell: Type I Lobar Pneumonia Treated with Concentrated Pneumococcic Antibody (Felton), J. A. M. A. 96: 1465 (May 2) 1931.

10. Bullowa, J. G. M., and Greenbaum, Evelyn: Pneumonia Due to *Pneumococcus* Type VII (Cooper), Arch. Int. Med. 60: 179-192 (Aug.) 1937.

11. Finland, Maxwell, and Tilghman, R. C.: Clinical and Immunologic Observations in Cases of *Pneumococcus* Type V Pneumonia Treated with Specific Antibody, New England J. Med. 215: 1211 (Dec. 24) 1936.

12. Lord, F. T., and Heffron, Roderick: Lobar Pneumonia and Serum Therapy, Commonwealth Fund, 1936.

However, every case seen in consultation was followed up for information concerning termination, complications and the like. Only cases in which the type of bacterial infection was definitely established are included in this group.

*Age and Sex Distribution.*—In the consultation series the average age and sex distribution was approximately the same as that noted in the private pavilion series.

*Distribution by Type.*—In table 7 the varieties of pneumonia are shown. The figures differ somewhat from those already presented for patients in private pavilions. In the consultation series the percentage of cases of pneumococcic pneumonia is lower and the incidence of cases of streptococcic and staphylococcic pneumonia is twice as high as in the private pavilion series. This difference was to be expected in a group of serious cases, such as those composing the consultation series.

*Incidence of Various Types of Pneumococcic Pneumonia in Consultation Series.*—In table 8 it will be noted that the incidence of the prevalent types of pneumococcic pneumonia does not differ widely from

than that for type III pneumonia (40 per cent) in city hospital clinics. Here again we must recall the age of the patients. One of the commonest types of patient encountered in consultation practice is the elderly patient with type III pneumonia, and a very high percentage of them die.

The fatality rate is also very high for the Streptococcus haemolyticus infections (50 per cent) and runs up to 100 per cent in the series of Staphylococcus aureus pneumonia (ten cases).

The fatality rate for patients with positive blood cultures was 70 per cent as compared with 42 per cent for patients with sterile blood cultures. A considerable number of patients with type III pneumonia died without developing sepsis, as in the pavilion series.

*Serum Therapy.*—Sixty-three patients with type I pneumonia received type I serum (table 9), with a fatality rate of 23.8 per cent, a figure practically identical with that for the serum treated patients in the private pavilion series. This rate is much too high for serum treated type I infections. In most of the large series studied from city hospitals the death rate for serum treated type I pneumonia has varied from 10 to 16 per cent.

The results of serum therapy in this series has been disappointing, chiefly because in nearly all cases the infections were severe to begin with, but more important still because many of these patients received serum late in the disease. For example, the death rate for sixty-three patients with type I infection who received serum was 23.8 per cent, while for sixteen patients who received no serum there was a fatality rate of only 25 per cent. However, for forty patients who received type I serum during the first three days of the disease there was a fatality rate of only 17.5 per cent. An analysis of the cases that were fatal in spite of serum treatment makes it quite obvious in most instances why the patient was not saved by the specific serum. For example, seven patients were treated after the fifth day and one patient was treated as late as the fourteenth day. Two patients had insufficient serum, one receiving only 6,000 units. Two patients died of pulmonary embolism after they had recovered from pneumonia. Two more were elderly alcoholic addicts.

What has been said concerning the type I cases applies equally to the type II series (table 9). The serum treatment again made a poor showing in a small group of cases. The number of cases of the higher types in which specific serum therapy was used is too small to be significant.

COMMENT

This study has provided a considerable amount of information concerning pneumonia in private practice. Of prime importance is the fact that the social stratum of the patient has little to do with the prognosis, which depends not so much on the economic status of the person as on his age, on the type of pneumonia and, most important of all, on the availability and early use of serum. With regard to the cost of antipneumococcus serum, its efficacy has now been so clearly proved that it should be supplied free by state and city boards of health, as is the case, for example, in the city and state of New York. It would appear from Rogers' figures that the death rate for pneumonia is lowest among patients who receive treatment at home. We imagine that the same will be found to be true in a similar study now being made by the health department in the city of New York.

TABLE 8.—Incidence and Fatality Rates of Pneumococcic Pneumonia in Consultation Practice (Serum Treated and Non-Serum Treated Combined)

Type of Pneumococcus	No. of Cases	Incidence, per Cent	Deaths	Mortality, per Cent
Type I.....	79	24.7	19	24.1
Type II.....	31	9.7	14	45.2
Type III.....	71	23.1	44	59.5
Miscellaneous types.....	136	42.5	49	27.7
Total.....	320	100.0	126	39.4

TABLE 9.—Fatality Rates of Consultation Patients Who Received Serum

Type of Pneumococcus	Received Serum	Died	Per Cent
Type I.....	63	15	23.8
Type II.....	27	13	48.1
Type III (rabbit serum).....	2	1	50.0
Miscellaneous types.....	16	5	31.3

that observed in the private pavilion series. Type III and the miscellaneous types compose a large percentage (65.6 per cent) of the group, just as in the private pavilion group.

*Complications.*—In this series of consultation cases, most of them severe infections, one would expect a rather high incidence of complications, and such proved to be the case. Empyema occurred in 12.6 per cent of all cases of type I pneumonia, with a death rate of 29.9 per cent, endocarditis in 1.1 per cent and meningitis in 0.85 per cent of all cases. Most of these consultation cases were seen in the home, with the family physician, and it is quite likely that a certain number of complications, such as terminal empyema, endocarditis and meningitis, were overlooked for lack of x-ray and other laboratory facilities.

*Fatality Rate.*—The case fatality rate for the entire series of consultation cases, including all types, both serum treated and non-serum treated cases, was 41 per cent, a very high rate and one that clearly indicates the serious prognosis in the group under consideration (table 7). In table 8 the case fatality rates for the dominant pneumococcus types are indicated. One is impressed with the high fatality rate for type III pneumonia, 59.5 per cent, which is considerably greater

One should not infer from this, however, that patients receive better treatment at home than they do in the private pavilions of hospitals. Nor should the inference be made that transportation in an ambulance is a detriment to the patient's chance of recovery. The Rockefeller Institute's statistics on pneumonia have always been among the best; yet practically every patient in their records was admitted by ambulance. The most plausible explanation is that the practitioner sends his sick patients to the hospital but allows his patients with mild attacks to remain at home. Certainly this seems the most rational explanation of the difference in death rates between home and hospital cases. At this point one may well raise the question of the proper disposition of the pneumonia patient in private practice. Should he be treated at home or should he be transferred to a convenient hospital? In answer to this question, several factors have to be taken into consideration:

1. Has the patient a comfortable home with proper facilities for handling the sick?
2. Does the patient live in town and at a convenient distance from the doctor's office or does he live in the country where he is inaccessible to emergency care?
3. Is the hospital under consideration provided with a medical house officer who is capable of handling medical emergencies such as vasomotor collapse, cyanosis or pulmonary edema?

There are certain obvious advantages in having a pneumonia patient under hospital care. The most important of these are that a clinical laboratory where sputum and blood cultures can be frequently examined is accessible; x-ray examinations are conveniently made; a house officer is usually available to handle any emergency that develops; oxygen therapy can be more readily supervised; serum treatment can be given at regular intervals, a procedure which is difficult to carry out in the private home, and, finally, if a surgical emergency arises, treatment can be promptly initiated.

Several facts brought out by this study are worthy of further comment. The fact should be stressed that the average age incidence of pneumonia among the well-to-do classes is almost a decade higher than that of pneumonia in the wards of large city hospitals. Pneumonia at Bellevue Hospital is a disease of young working men; pneumonia in private practice is a disease of the middle aged and elderly.

Certainly one of the most interesting facts elucidated has been the very high incidence and death rate of patients in private practice with type III pneumonia. Type III pneumonia, by reason of its prevalence and fatality rate of almost 60 per cent, has come to be one of the most serious problems that the practitioner has to face. It is made doubly serious by reason of the apparent failure of type III serum to control the infection.

It was disappointing to find so many histories of private patients with pneumonia in the hospital files with no record of any bacteriologic study. However, this investigation covers a period of ten years. During the last five years, sputum typing and blood cultures have been carried out in a much higher percentage of cases. This applies also to the use of antipneumococcus serum in the treatment of type I pneumonia. Only 60 per cent of the patients with type I pneumonia in the private pavilion series received type I serum. However, the percentage of cases in which serum therapy was used is definitely higher for the last five years of the study than for the first five years. With respect to the series of 351 cases of pneumonia in the con-

sultation series, the fact should be stressed that we are dealing here with a group of very ill patients. The fatality rate in this group was quite high for every type. The lesson to be derived from a study of this group is that consultations should be held early in the disease, when special therapy such as oxygen and serum will be of most value to the patient.

Pneumonia in private practice is not so mild a disease as it has often been considered to be. Certainly in New York private hospital pavilions the fatality rate is surprisingly high—no doubt definitely higher than the rate for small towns and rural districts.

We regret that we cannot speak with more authority concerning the value of serum in the treatment of the newer types of pneumonia. Our impressions have been quite favorable, particularly in the serum treatment of types V, VII and VIII, but the number of cases observed is too small to have statistical value.

We have omitted statistical data on the dosage of serum administered, since accurate details were not always available from the patient's chart. In nearly every case the serum employed has been of the concentrated and refined type of horse serum first described by Felton. The new method of giving serum in large single intravenous doses of from 100,000 to 150,000 units seems to have no deleterious effects when given very slowly, but we agree with Lord and Heffron that it is still wiser for the general practitioner to administer serum in frequent divided doses.

Only fifteen patients in our entire series were treated with antipneumococcus rabbit serum. Because of the small number of cases in this group, we have refrained from drawing any conclusions. However, apart from the fact that rabbit serum is available for some types for which there is at present no horse serum (types VI, XVII, XVIII and so on) we have found no noteworthy difference either in the course of the disease or in the incidence of complications when compared with those treated with refined horse serum. In a patient with type III pneumonia who received approximately 850,000 units of concentrated type III rabbit serum early in the disease there developed, several days after administration of serum, a pneumococcus type III empyema necessitating resection of a rib.

#### SUMMARY

1. Nine hundred and eleven cases of pneumonia from the records of private practice were reviewed with special reference to the incidence and fatality rates for the various types and the results of serum therapy.
2. The data obtained from the "private practice" series were compared with well established data based on pneumonia records from the public wards of large city hospitals.
3. The most significant facts brought out by this comparative study are:
  - (a) The generally higher age incidence of pneumonia in the well-to-do classes.
  - (b) The high incidence of type III pneumonia in private practice. This probably results in part from the higher age incidence of this group.
  - (c) Inadequate bacteriologic study of the "private pavilion" cases. Less than half of the patients available for study had been properly typed.
4. Only 60 per cent of the private pavilion patients with pneumococcus type I infections received type I serum. In the "consultation series" a much higher proportion received serum. The results of serum therapy in both series were not as favorable as those obtained

in the general wards of large city hospitals; the fatality rate of 23.5 per cent for the entire series of 115 cases of type I pneumonia in which serum therapy was given is almost double that reported from various other sources and is not conspicuously lower than the standard fatality rate (30 per cent) for type I non-serum treated cases. A number of factors, such as the higher age incidence, the severity of the cases studied, delay in administering serum, or inadequate dosage are probably responsible for this high figure.

5. Pneumonia in private practice is not so mild as it has often been claimed to be. In view of the well demonstrated value of specific therapy in pneumonia, administration of serum should be part of the routine treatment in every case amenable to such therapy, regardless of the social status of the patient.

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## THE TOXEMIAS OF PREGNANCY

TREATMENT BASED ON A NEW CONCEPT  
OF THE ETIOLOGY

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A new concept of the physiology and pathology underlying the development of the toxemic state in pregnancy is based on old and new knowledge of the role of body fluids in maintaining the integrity of the organism. A method of treatment is derived from this concept in the light of facts developed in connection with studies on water balance, acid-base equilibrium, renal function and shifts in body water and electrolyte.

Newburgh<sup>1</sup> and his associates have measured water exchange in many persons with normal and abnormal renal function. They found that if the intake of water was restricted in cases of impaired renal function, retention of urinary solids would result. If large amounts of water were given, the quantity of urinary solids excreted would be comparable to the excretion by a normal person ingesting the same diet. From these data they were able to calculate the amount of urinary water necessary to remove definite quantities of urinary solids. As the concentrating ability of the kidneys lessened, more urinary water was necessary to remove the urinary solids.

Fluid is held within the body in two main chambers, the extracellular and the intracellular compartment. The cells of the body are surrounded by interstitial fluid. This fluid carries nourishment to, and waste away from, the cells. It also controls the temperature of the organism and maintains osmotic equilibrium and a stable hydrogen ion concentration.

The fluid contained in an organism amounts to approximately 70 per cent of the body weight. The extracellular fluid accounts for 20 per cent and the intracellular for 50 per cent. The extracellular fluid

is composed of the blood plasma 5 per cent and the interstitial fluid, including lymph, 15 per cent of the body weight. In a person weighing 150 pounds (68 Kg.) the body fluid would be distributed approximately as in table 1.

Darrow and Yannet<sup>2</sup> found that when there was an increase in extracellular electrolyte there was a shift of body water from the cells to the extracellular fluid but that when there was a decrease in extracellular electrolyte there was a shift of water from the extracellular fluid into the cells. They pointed out that, as nine tenths of the osmotic pressure of body fluids is maintained by electrolyte, the shift of body water is largely governed by the distribution of electrolyte.

When urinary solids are retained there is an accumulation of both urinary waste and electrolyte in the blood plasma. It then becomes necessary for the organism to make adjustments to maintain osmotic equilibrium and to keep the hydrogen ion concentration within normal limits if normal metabolic activity is to persist. Small molecules and inorganic ions pass readily across the capillary membrane into the interstitial spaces. The interstitial fluid, in order to maintain osmotic equilibrium with the intracellular fluid, draws water from the cells. Darrow and Yannet<sup>2</sup> emphasized the fact that, when the concentration of electrolyte in the extracellular fluid is altered, serious symptoms can follow the shift of body water from the cells to the extracellular fluid even though the total body water is unchanged.

Gamble<sup>3</sup> pointed out that in considering electrolyte one deals not with salts but with separately controlled concentrations of anions and cations. Therefore when retention of urinary solids is present a consideration of the food ingested is of great importance. The average diet composed of liberal quantities of milk, fruits and vegetables yields a basic ash. If when retention occurs the diet ingested yields a basic ash, there will be an increase of base in the blood plasma. Ordinarily the kidneys control the amount of base in the blood, but if renal function is hampered and excess base is not eliminated the excess base must move out of the blood plasma into the interstitial fluid to preserve a normal hydrogen ion concentration. This shift produces edema, or swelling, of the interstitial spaces, and shrinking, or dehydration, in the cells.

If the diet yields an acid ash and the excess ions cannot be excreted, the lungs will dispose of carbonic acid, thus keeping acid and base in balance. Clinical edema will not be noted. This protective mechanism alters the composition of the blood plasma, and gradually an important buffer, bicarbonate, is depleted and replaced by acid ions which should have been excreted. A serious toxemia, with no appreciable edema, may develop.

Newburgh<sup>4</sup> has developed a diet the ash of which gives a neutral reaction. By using this diet he is able to supply ample food without disturbing the delicate acid-base balance.

### THE TOXEMIAS

It is believed that toxemia will not develop if no impairment of renal function exists. The impairment may be so slight that no test yet developed will point

From the Great Falls Clinic.  
Read before the Section on Obstetrics and Gynecology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

1. (a) Newburgh, L. H., Wiley, F. H., and Lashmet, F. H.: A Method for the Determination of Heat Production Over Long Periods of Time, *J. Clin. Investigation* 10: 703-721 (Oct.) 1931. (b) Wiley, F. H., and Newburgh, L. H.: An Improved Method for Determination of Water Balance, *J. Clin. Investigation* 10: 723-731 (Oct.) 1931. (c) Lashmet, F. H., and Newburgh, L. H.: A Comparative Study of Excretion of Water and Solids by Normal and Abnormal Kidneys, *ibid.* 11: 1003-1009 (Sept.) 1932. (d) Newburgh, L. H., and Lashmet, F. H.: The Importance of Dealing Quantitatively with Water in the Study of Disease, *Am. J. M. Sc.* 186: 461-471 (Oct.) 1933.

2. Darrow, D. C., and Yannet, Herman: The Changes in the Distribution of Body Water Accompanying Increase and Decrease in Extracellular Electrolyte, *J. Clin. Investigation* 14: 266-275 (March) 1935.  
3. Gamble, J. L.: Extracellular Fluid, *Bull. Johns Hopkins Hosp.* 61: 151-173 (Sept.) 1937.  
4. Newburgh, L. H., and MacKinnon, Frances: The Practice of Dietetics, New York, MacMillan Company, 1934, chapters 11 and 13.

it out. However, when the burden of fetal excretion is added without a sufficient increase in fluid intake there may be a retention of urinary waste and electrolyte. As the blood plasma is not able to rid itself of these retained products it becomes hypertonic. In order that osmotic equilibrium may be retained there must then be a shift of water from the reservoir of the body, the intracellular compartment. This shift of water will at first aid in the excretion of some of the retained solids; but, as the retention increases, some of the small molecules and inorganic ions will pass into the interstitial spaces. More water is then drawn from the cells to maintain osmotic equilibrium with the surrounding fluid.

The changes within the body will be influenced by the reaction of the residue after the food is burned. A diet yielding an alkaline ash will produce a shift of water from the cells to the interstitial spaces. The result is cellular dehydration and edema. If the diet yields an acid ash, water will be drawn from the cells to increase the urinary output. The result is an increased concentration in the intracellular and extracellular fluid. In both instances metabolic activity is altered by increased concentration within the cells.

#### TREATMENT OF THE TOXEMIAS OF PREGNANCY

Newburgh<sup>1c</sup> demonstrated that impaired kidneys could be made to excrete the normal amount of urinary solids if large amounts of fluid were ingested. Treatment of the toxemic patient must vary for the non-convulsive and the convulsive type, yet the basic principle remains the same. To overcome the retention of urinary solids large quantities of fluid must be ingested. As fluids are taken liberally the blood plasma becomes hypotonic. In other words, the osmotic pressure of the blood plasma is less than that of the interstitial spaces. As a result, water will pass to the interstitial fluid and small molecules and inorganic ions will pass into the blood plasma. The interstitial fluid, then maintaining osmotic equilibrium with the intracellular fluid, gives up water to the cells and the cells are hydrated.

A great deal can be done to prevent the toxemias of pregnancy. Newburgh<sup>1c</sup> has found that impaired kidneys do not produce a highly concentrated urine even though the intake of water is restricted. Dieckmann<sup>5</sup> reported the mean for the maximum specific gravity in normal pregnancy to be 1.022. A patient not ingesting a great deal of fluid and excreting urine having a specific gravity of 1.020 or lower should be considered to have some retention of urinary solids. The presence of renal epithelium in the urinary sediment suggests renal damage.

The treatment of mild toxemia is simple, and progress of the toxemia may be averted. The success of the treatment depends on the cooperation of the patient. Fluids are forced. A urinary output of 2,500 cc. will be ample unless great renal impairment exists. A neutral diet is prescribed. This may be devised from the list of foods prepared by Newburgh.<sup>4</sup> As sodium is a predisposing cause of edema, foods having a low sodium content are chosen, and for the same reason sodium chloride and sodium bicarbonate are eliminated.

Severe nonconvulsive toxemia is treated in a similar manner. The patient should be observed more closely, because of the severity of the symptoms. Hospital

care is of great value. The patient with severe pre-eclampsia may be treated over a long time if large quantities of fluids are given and if the urinary output is maintained large. A neutral diet is necessary, as is acid base equilibrium.

In the case of the convulsive toxemias, fluids cannot be given by mouth; therefore a parenteral route must be chosen. Fluids are more rapidly absorbed when given intravenously, but the subcutaneous method of administration is also valuable. The object is to give large amounts of fluid. Eichelberger and Hastings<sup>6</sup> have demonstrated that hypertonic dextrose solution dehydrates the cells. They found that isotonic dextrose solution would make water available to the cells. Therefore as the cells are already dehydrated and as hypertonic dextrose solution will increase that dehydration, isotonic dextrose solution is given.

The amount of fluid necessary may be determined roughly. Collier and Maddock<sup>7</sup> found that a dehydrated patient had lost 6 per cent of body weight. A convulsive patient weighing 150 pounds (68 Kg.) should have the following needs considered in the first twenty-four hours: water to hydrate the cells, 4,100 cc.; urinary water, 3,000 cc.; vapor water (skin and lungs), 1,000 cc.; total, 8,100 cc. A large estimate must be made for urinary water if the kidneys are to excrete large amounts of retained urinary solids.

TABLE 1.—Distribution of Body Fluid

Extracellular fluid.....	13,600 cc.
Blood plasma .....	
.....	34,000 cc.
Total.....	47,600 cc.

Very little medication is necessary even though convulsions are present. Usually an initial intramuscular injection of soluble phenobarbital will control the convulsions until intravenous treatment is instituted. It has not been necessary to repeat this medication, as the irritability disappears as fluids are given.

Two thousand cc. of 5 per cent dextrose solution may be given intravenously in about two hours. After 1,000 cc. has been given, the administration of 5 per cent dextrose solution by hypodermoclysis is started. A total of 4,000 cc. of the solution is given in about eight hours. The fluid given subcutaneously is absorbed very rapidly. Diuresis is not expected immediately, as available water will first replace that lost by the dehydrated cells. Within twelve hours it is unusual if a patient will not drink water when encouraged. Water is given freely by mouth, but only water. It is usually necessary to give fluids by the parenteral route for several days before a patient will take enough by mouth.

It is generally true that a patient treated in this manner will regain consciousness before renal excretion is reestablished. It seems logical to deduce that all the cells of the body are in such urgent need of water that many processes are suspended. As the cells are hydrated, those processes are resumed. Convulsive patients are not given food until after three days of freedom from convulsions. They are then treated as patients with severe nonconvulsive toxemia.

6. Eichelberger, Lillian, and Hastings, A. B.: The Exchange of Salt and Water Between Muscle and Blood, *J. Biol. Chem.* 118:197-204 (March) 1937.

7. Collier, F. A., and Maddock, W. G.: A Study of Dehydration in Humans, *Ann. Surg.* 102:947-960 (Nov.) 1935.

5. Dieckmann, W. J.: Renal Function in the Toxemias of Pregnancy, *Am. J. Obst. & Gynec.* 29:472 (April) 1935.



COMMENT

Starling<sup>8</sup> emphasized first in 1896 and later in 1908 the important relationship between disease and the physiology of body fluids and their electrolytes and colloid osmotic pressures. Since that time his theories have been confined by Darrow and Yannet, Gamble, Peters, Landis, Hastings, Eichelberger and others. Starling noted that the important function of the kidneys is to regulate the amount and composition of the total fluid in the body. If by some change in that function the molecular concentration of the fluid surrounding the cells of the body is altered, it is necessary for the cells to give up or take on water until the osmotic pressure within the cell is equal to that of the extracellular fluid.

Newburgh<sup>10</sup> has demonstrated that a liberal fluid intake is necessary for the proper excretion of urinary solids in persons having impaired renal function. When fetal metabolism increases the normal amount of urinary

TABLE 2.—Summary of Maternal and Infant Mortality for Toxemias of Pregnancy in Cases in Which the Infant Reached a Period of Viability

Date	Antepartum Observation	Cases	Infants	Maternal Mor-tality	Infant Deaths and Still-births	Infant Mor-tality, Per-centage
Nonconvulsive, All Types						
1931-1935 1,000 deliveries; treatment conservative	Yes.....	45	46	0	3	6.5
	Not treated until toxemia was severe	7	8	0	3	37.5
1935-1938 1,000 deliveries; treatment, forced fluids, neutral diet	Yes.....	53	54	0	1	1.8
	Not treated until toxemia was severe	6	7	0	4	57.0
Convulsive Type						
1931-1935.....	Yes.....	2	2	0	0	0
	Not treated until toxemia was severe	4	6	0	2	33.3
1935-1938.....	Yes.....	0	0	0	0	0
	Not treated until toxemia was severe	0	0	0	0	0

solids, retention may occur as a result of insufficient urinary water. Because of the great reservoir in the interstitial spaces much of the retained material can immediately be removed from the blood plasma so that osmotic equilibrium is maintained. Studies of the blood chemistry do not then reveal a true picture of the retention process.

When retention of urinary solids occurs, the preservation of a normal range in hydrogen ion concentration is a vital necessity. If the diet yields a basic ash, as a diet containing large amounts of fruits, vegetables and milk will, a large part of this excess base must be withdrawn from the blood plasma to prevent alkalosis. A diet rich in cereals and meat will yield an acid ash. The excess acid must be removed or acidosis will result.

The treatment then should be based on removing the retained solids from the organism rather than on neutralizing them, or on treating separate symptoms, such as edema, cerebral manifestations and blood pressure. Large amounts of fluid taken over many days will promote a copious renal output. When the toxemia is of the nonconvulsive type this water may easily be taken by mouth. Most patients will ingest 5,000 cc.

a day with only a little encouragement. In order to avoid the ingestion of any excess acid or base, a neutral diet is given.

In treating eclampsia, control of the convulsions is necessary. This control may be obtained by soluble phenobarbital given intramuscularly. As soon as the convulsions are controlled fluids may be given. The intravenous method is the method of choice at first. Eichelberger and Hastings<sup>9</sup> found that hypertonic dextrose solution produces prompt diuresis but dehydrates the cells. It will not produce a permanent urinary output. There is often a depletion of glycogen in the toxic patient, so at first a large amount of dextrose solution may be utilized. So long as that utilization takes place some water will be liberated to overcome cellular dehydration, but little will be accomplished in removing retained urinary solids. Isotonic dextrose solution, on the other hand, liberates large quantities of water when the sugar is burned.

During the development of toxemia, water is withdrawn from the cells to furnish diluent for excess electrolyte and retained solids. The cells then become concentrated. This increased concentration is in osmotic equilibrium with the extracellular fluid, but the concentration produces a pathologic state within the cells. It is well known that an organism can survive with no food for a long period but that when water is restricted life is limited. The vital part of the organism, the cells, becomes dehydrated under conditions which draw water from the intracellular compartment. This process alters cellular function and endangers life.

De Snoo<sup>9</sup> reported unusually excellent results in preventing eclampsia by the use of a salt-free diet and fluids. He attributed the cause of the convulsion to salt rather than to a physicochemical change in the relationship between the blood plasma, the interstitial fluid and the intracellular fluid. Failure to consider the reaction of the residue of the diet will account for the rare failure of his treatment.

The milk diet has gradually been abandoned by many obstetricians because it apparently instituted convulsions. Milk yields an alkaline ash but, if with each glass of milk one and one-half slices of salt-free bread are ingested, an ideal neutral diet is provided. With this diet many patients may be treated at home without the help of an expert dietitian.

The dehydration therapy of Arnold and Fay has been used successfully by the originators. Over a long time, serious damage to tissues must result unless sufficient water is given to allow the kidneys to excrete all the urinary solids. However, when a dry diet is used as they specify, it must of necessity yield an acid ash. This diet would be of great value for a patient having gross edema, as much of the edema fluid would be liberated to provide sodium ions to maintain a normal hydrogen ion concentration. For patients having no edema and other signs of toxemia, the treatment is dangerous.

The action of magnesium sulfate is not known. Stander<sup>10</sup> found in experimental work that magnesium sulfate produced moderate necrosis in the central part of the lobule of the liver and moderate degeneration in the convoluted tubules of the kidneys. As serious damage to the liver and kidneys may result from the

8. Starling, E. H.: The Herter Lectures on the Fluids of the Body, Chicago, W. T. Keener & Co., 1909.

9. de Snoo, K.: The Prevention of Eclampsia, *Am. J. Obst. & Gynec.* 34: 911-939 (Dec.) 1937.  
10. Stander, H. J.: Effect of Intravenous Administration of Magnesium Sulfate, *Tr. Sec. Obst., Gynec. & Abdom. Surg., A. M. A., 1928*, pp. 210-224.

toxemia alone, it seems unwise to use a drug which may increase the damage. It is possible that magnesium sulfate may be most valuable by furnishing the acid  $\text{SO}_4$  ion.

Most low protein salt-free diets are unsuccessful because the ash is strongly basic. If the diet was designed to yield a neutral ash it would be satisfactory.

Recently great emphasis has been placed on plasma proteins. Darrow and Yannet found that electrolyte accounted for about 90 per cent of the osmotic pressure exerted by body fluids. They also found that when electrolyte was increased the plasma proteins decreased. When the extracellular fluid is made hypertonic by retained urinary solids and electrolyte, water is drawn from the cells to maintain osmotic equilibrium between the intracellular and the extracellular fluid. The extracellular fluid is diluted by the additional water and the plasma proteins will be relatively decreased. It is not easy to increase the plasma proteins by diet, but they may be increased by removing excess electrolyte, by the ingestion of large amounts of water.

By following the treatment outlined it is possible to treat patients having considerable tissue damage, provided enough water is ingested to allow impaired kidneys to excrete retained urinary solids. It must constantly be borne in mind that the cells will be dehydrated to some extent when edema exists. Therefore a successful treatment should point first toward hydrating the cells and second toward promoting urinary excretion. The fact that coma disappears before urinary excretion becomes normal when fluids are given freely suggests that cellular dehydration has an important role in the pathologic process of the toxemias of pregnancy.

This treatment will control the development of severe toxemia, making it unnecessary to induce labor in a seriously toxic patient until after the toxemia is under control. The maternal risk is greatly decreased, and in addition the fetal mortality is lessened. The modern tendency to induce labor as toxemia becomes more severe leads to a low maternal mortality, but many babies are lost as a result of fetal toxemia and prematurity. A successful method of treating the toxemias of pregnancy should be productive of a low fetal mortality as well as a low maternal mortality.

The result of treating the toxemias in 2,000 consecutive deliveries is presented in table 2. The toxic patients were divided into two groups. The group seen for the first time with severe toxemia was eliminated as having had no antepartum care. In most instances fetal heart tones were not heard when the patient was admitted; therefore treatment had no bearing on the fetal mortality.

In the group receiving antepartum care an interesting comparison is possible. One thousand patients were delivered between Aug. 1, 1931, and June 1, 1935. Forty-five had a nonconvulsive toxemia. The fetal mortality was 6.5 per cent. Two patients had eclampsia. Only one convulsion was recorded for each patient. The treatment in this group was conservative. Fluids were given in moderate amounts, and the diet was low in protein and salt. No attention was paid to the reaction of the diet, and it consequently yielded a basic ash. Labor was induced if the toxemia became more severe.

A second group of 1,000 patients was delivered between June 1, 1935, and March 20, 1938. Fifty-three had a nonconvulsive toxemia. There were no convulsive patients. The treatment was as outlined in

this paper. Fluids were forced, and a neutral diet low in sodium was given. The fifty-three mothers were delivered of fifty-four babies. One baby, a fetal monstrosity, was lost, so that the fetal mortality was 1.8 per cent.

#### SUMMARY

1. The toxemias of pregnancy occur in women with some previous impairment of renal function. This impairment leads to a gradual retention of urinary waste and electrolyte.

2. Retention of urinary solids leads to dehydration of all the cells of the body and the fetus. Dehydration alters the function of the cells and accounts for metabolic changes in the various organs of the body.

3. Retention of electrolyte is responsible for the different types of toxemias. A diet yielding an alkaline ash leads to retention of alkaline ions and the development of cellular dehydration in the presence of edema. A diet high in acid ash leads to retention of acid ions with general dehydration of all cells.

4. The toxemias may be prevented by the ingestion of large quantities of fluid and a neutral diet low in sodium if treated early, or they may be controlled at any time if treated before severe cellular damage has resulted.

5. The infant mortality for the toxemias of pregnancy can be lowered.

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#### ABSTRACT OF DISCUSSION

DR. P. J. CARTER, New Orleans: Dr. McPhail's paper is in keeping with the present day treatment of the toxemias of pregnancy. I agree that urinary solids should never be allowed to be retained on account of the accumulation of urinary waste and electrolyte in the blood plasma, as a result of impaired renal function. An attempt to secure a neutral ash is important, for if renal function is hampered a disturbance in water balance may occur with a resulting toxemia. The mechanism by which water is displaced or added to in a toxic individual and the reaction of the tissues and cells to such a toxemia are excellently outlined in Dr. McPhail's paper. The effect on the kidney shows the most striking abnormalities in toxemia; it is believed that toxemia will not develop when no impairment of renal function exists. The adage "dehydrate in edema" has well stood the test, and the proper use of the tonic solutions of dextrose has been our greatest accomplishment in lessening the maternal and fetal mortality in the toxemia of pregnancy. In our present knowledge of cell activity whereby little or no edema occurs when water becomes bound up in the cell protoplasm, as against visible edema when the fluid accumulates in the intracellular spaces, we have an important factor influencing water balance. I cannot agree with Dr. McPhail in giving 2,000 cc. of 5 per cent dextrose solution intravenously in about two hours, with a total of about 4,000 cc. in about eight hours. This seems to me an excessive amount of water to give a patient in eclampsia, in which the heart action has been disturbed and disabled, and this amount would tend to cripple its action still further. My observations through the Charity Hospital at New Orleans, where we have an abundance of material, have been that eclamptic patients fare better with a lesser amount of concentrated solution at longer intervals; namely, 500 cc. of a 20 per cent solution intravenously every six hours or even in a greater concentration in the individual case. In the toxemias of pregnancy we are still treating the symptoms of a disease of little known origin, but which reveals to us a disturbed water balance in which an excessive intake or output results in the accumulation in the intracellular spaces of water producing edema, or accumulating in the cells with little or no edema. In summing up, the salt element and its concomitant reactions with retention and storage of chlorides play a most important part in the development of pregnancy toxemia. One cannot begin to attain a proper water balance and a proper ratio in osmotic pressure, which are essential in the treatment



of this disease, when one loads the overburdened tissues and cells with additional water and excess of electrolyte.

DR. LYLE G. McNEILE, Los Angeles: I congratulate Dr. McPhail in presenting a new concept of the etiology of the toxemias of pregnancy and the development of a treatment based on a new concept. Any theory, however, must establish beyond question the premises on which it is based. It appears to me that in order for Dr. McPhail to establish his case he must either assume or prove certain facts. First he must prove that there is renal impairment in all cases of toxemia. Delicate clearance tests of kidney function in the toxemias have frequently failed to disclose such impairment. Secondly he must demonstrate that the degree of renal impairment must be sufficient to cause a retention of electrolytes (sodium, potassium, chloride and the like as well as urinary solids). In the early stages of eclampsia there almost always is no impairment of the concentrating power or of the ability of the kidneys to excrete electrolytes. The concentration of the urine during the phase of acute oliguria is usually over 1.030. Page, in my clinic, has made numerous Addis tests of concentrating power in selected cases of severe eclamptogenic toxemias and has failed to obtain specific gravities of less than 1.026 on any of them after from eighteen to twenty-four hours of dehydration. The work of Newburgh and others quoted by Dr. McPhail refers only to the amount of water required to excrete urinary solids when there is a known impairment of concentrating powers of the kidney. Dieckmann, Killian and Stander, moreover, have found that the concentration of electrolytes in the blood of eclamptic patients is within the normal range. The author answers this in his paper by stating that blood chemical studies do not always reveal "a true picture of the retention process." As affecting certain phases this may be true, but in the matter under discussion it is hardly true, for the electrolytes are freely permeable through capillaries and are in constant equilibrium between the blood and extracellular fluids. Thirdly the proponent of this theory must show that such a retention of electrolytes would lead to a "cell dehydration" without producing general dehydration. Darrow and Yannet state that the loss of electrolytes produces the symptoms and signs of dehydration but that an increase of extracellular electrolytes experimentally leads only to the symptom of extreme thirst. I have never noted such pathologic thirst as a symptom of toxemia. Is it true that the blood in eclampsia becomes hypertonic? Harden and his associates, Seitz, and the authors of the first paper on our program seem to have demonstrated that the blood may become hypotonic through loss of albumin in the urine. This would lead to cell hydration rather than cell dehydration. Most important, a proponent of this theory must show that cell dehydration would lead to a suspension of cell function or to any of the symptoms of eclampsia.

DR. FRANCIS L. MCPHAIL, Great Falls, Mont.: Darrow and Yannet noted dry mucous membranes and increased thirst in animals after increasing the extracellular electrolyte. In experiments a large amount of salt was injected into small animals. When a retention process develops in pregnancy it develops slowly and the extracellular electrolyte is probably increased to a lesser degree. Nevertheless the mucous membranes appear dry in many toxic patients. If 500 cc. of 20 per cent solution of dextrose is given, very little water will pass into the cells. While glycogen depletion is present in the toxemic state, a concentrated solution of dextrose may be utilized, but as glycogen is replaced in the tissues only a small amount of dextrose is oxidized and little water is liberated to hydrate the cells. A method of treatment has been presented which has worked well in the prevention and treatment of eclampsia and in the treatment of severe nonconvulsive toxemias. It does not depend on polypharmacy. Adequate renal excretion and restoration of function have resulted. The value of the treatment may be determined after a fair trial.

**Duration of Life in Sixteenth Century.**—In the sixteenth century the average duration of life was eighteen years. Fully one-half the population of every country died under the age of twelve, and 60 per cent of those died before their fifth year.—Hurd-Mead, Kate Campbell: *A History of Women in Medicine*, Haddam, Conn., the Haddam Press, 1938.

## RELATION BETWEEN BLOOD PLASMA PROTEINS AND TOXEMIAS OF PREGNANCY

A PRELIMINARY REPORT

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Diets for pregnant women are not modern, though their use in the past was more empiric than scientific. The angel in Biblical times gave the father of Samson instructions before his birth, saying "She may not eat of anything that cometh from the vine, neither let her drink wine or strong drink nor eat any unclean things" (Judges 13:14). Since then each generation has added or subtracted, restricted or insisted, on a variety of foods. The textbooks of the middle nineteenth century have practically no antepartum advice and only mention that an adequate diet should be prescribed for convulsions without saying what constitutes an adequate diet.<sup>1</sup> Even as late as 1928 De Lee,<sup>2</sup> in his antepartum instructions concerning diet, did not advocate a balanced diet. He advised that the patient "omit meats and broths and limit eggs and fish." Curtis,<sup>3</sup> with two full pages on diet, said "Meat is to be taken moderately." This is an advance toward balancing the diet. Beck,<sup>4</sup> however, hewed to the conventional diet of the past—the decreasing of proteins during the latter part of pregnancy and the restricting of proteins in the case of toxemia, the animal proteins being replaced with vegetable proteins.

Several years ago it became evident to one of us that certain patients in the antepartum clinic of the City Memorial Hospital of Winston-Salem, N. C., who had edema or high blood pressure seemed to improve clinically even though they continued to eat meats when instructed to abstain. As this was before an increase of protein in the diet was beginning to be advocated, it was thought best to stress a salt-free and porkless diet, omitting the restriction of other proteins but urging, as before, that more milk be taken. Many patients volunteered the information that they ate beef and eggs, and these were not restricted in amount. With this diet there were no cases of eclampsia in the clinic in four years, though previously there had been several cases each year.

During a conference with Strauss in Boston in 1936 we mentioned the fact that, while we did not advocate the use of proteins during the latter part of pregnancy or in cases of toxemia, we did not restrict them and our patients were consuming varying amounts with no apparent harm. Strauss at this time was studying the effect of very high protein diets on toxemia, diets with 260 Gm. of protein daily, in the form of milk, lean meats and egg whites. His patients lost weight, their blood pressure fell, the subjective symptoms abated and

Mr. Walter Mickle cooperated in the laboratory determinations. Read before the Section on Obstetrics and Gynecology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

1. Meigs, Charles D.: *Treatise on Obstetrics: The Science and Art*, ed. 2, Philadelphia, Lea & Blanchard, 1852.
2. De Lee, Joseph B.: *Principles and Practice of Obstetrics*, ed. 5, Philadelphia, W. B. Saunders Company, 1928.
3. Curtis, A. H.: *Obstetrics and Gynecology*, Philadelphia, W. B. Saunders Company, 1933.
4. Beck, A. C.: *Obstetrical Practice*, Baltimore, Williams & Wilkins Company, 1935.

in some cases the albuminuria was decreased. These had been the effects, to a lesser degree, with some of our patients when they had taken protein against our instructions. We planned to give some of our clinic patients an increased protein intake, as a routine, to see how they would react. Because of the low economic status of our patients and our lack of hospital beds for experimental work we arbitrarily decided on six whole eggs a day in addition to the 1 or 2 quarts of skim milk and the legumes which they might have. They were told to eat whatever meat they had, aside from salt pork. Knowing that an increase of protein was against previous training, we did not feel it wise to omit the magnesium sulfate when indicated and insisted that they use a salt-free diet. Most of the patients reported that they felt so much better and a few of the toxemias improved so dramatically that it became a routine to have the patients add six or eight whole eggs to their daily diet. One of the first patients given this diet was a Negro girl aged 14, seen in one of our rural antepartum clinics. She was eight months pregnant, had a blood pressure of 190 systolic, 110 diastolic, a 2 plus reaction for albumin, and edema, with headache and dizziness, and appeared very stupid. She was put on the old routine of a low protein diet, with from 2 to 3 quarts of skim milk daily, rest in bed and magnesium sulfate. At the next clinic, two weeks later, she had gained 10 pounds (4 Kg.), appeared more stupid and had a blood pressure of 200/115. Both the mother and the nurse who had seen her during the past two weeks assured us that she had followed instructions. We added from eight to ten whole eggs to the milk, thus giving her around 90 Gm. of protein a day. The family lived in the country and had enough eggs for her. When seen two weeks later she had lost 10 pounds, was very clear mentally and had a blood pressure of 140/90 and no albuminuria. She was delivered spontaneously before her next clinic visit, without any evidence of toxemia appearing during or after labor.

It was about this time that Harden's<sup>5</sup> monograph was brought to our attention. In his cases he attempted to maintain a positive balance of nitrogen in order to supply the fetal requirements without depleting the maternal proteins. He calculated the amount of protein required in the cases of toxemia by adding to the minimum amount required for maintenance 50 Gm., the amount of protein metabolized, as evidenced by the end products in the urine and the estimated requirements of a 2 kilogram fetus. His patients averaged from 75 to 80 Gm. of protein daily. Though we had chosen our amounts arbitrarily, we found that we had been giving approximately the same amounts as Harden. In a four year series he<sup>6</sup> found that none of the 522 patients given his protein stabilization diet had had convulsions, while the frequency of convulsions in referred cases in the locality remained the same. Our experience has been similar, as will be shown.

Our empirically chosen amounts of protein and the calculated amounts of Harden were considerably less than the amounts given by Strauss. While our clinic patients were having no eclampsia, some were having toxemia, though it was milder in those who were able to obtain the milk and eggs. Were the toxemias of our patients who subsisted on turnip greens, sweet pota-

toes and corn bread, with occasionally fresh fish and pork, due to a lack of protein or to an improperly balanced diet, which needed a positive balance of other nutritive factors required by the fetus? We determined to estimate the blood plasma proteins of a series of patients who were receiving the type of diet which they would have had if they had not been pregnant or had had no instructions in diet to see whether there was a significant change in plasma proteins. These patients were instructed to eat and live as they had before they knew that they were pregnant. As we had previously been urging them to increase the proteins by adding milk, eggs and cheese to the diet and to cut down the salt intake, we did not begin to collect the specimens of blood until after they had been on their new diet for at least a week. They were told to take no magnesium sulfate and to eat the same amount of salt they usually did, as well as to prepare the food with seasoning meat.

The plasma proteins of the blood of thirty-four non-pregnant women of the same social status from the clinic were used as controls.

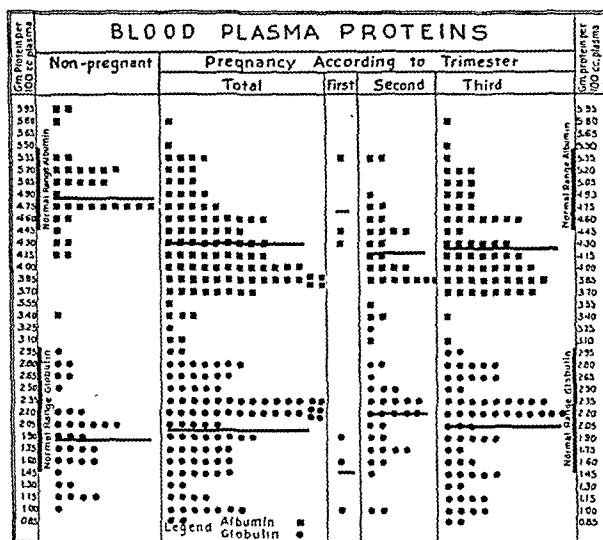


Chart 1.—Plasma albumin and globulin concentrations for thirty-four nonpregnant women of the same economic status as the pregnant women, for the pregnant women as a group and for the pregnant women by trimester. In the charts each square and circle represents one determination, and the horizontal lines represent the average values for each group. (See text for probable error of means.)

Persons who have worked with clinic patients realize that they cannot be controlled like guinea pigs in cages. However, in choosing the patients for this study we tried to make sure that those classified as having a normal pregnancy or receiving a regular diet were not getting a high protein intake. Some of the patients in this group should probably be included in the high protein group, as we had a feeling that they were eating more protein than they would admit. This is easy to understand, because, having been on an adequate protein diet previously, they did not feel as well with a restricted protein intake. As a result of this our figures may be somewhat higher than they ought to be, particularly for the third trimester.

The albumin and globulin were determined by the method of Bowman. It was thought well to divide the pregnant patients according to the three trimesters and to group together those who we were certain were on a high protein diet and those who had toxemia. The patients with toxemia all had a blood pressure of 145/100 or higher and were known to have had a nor-

5. Harden, Boyd: A Study in Pre-Eclampsia and Eclampsia, Pittsburgh, University of Pittsburgh, 1936.

6. Harden, Boyd: Clinical Management of Pre-Eclampsia and Eclampsia, Pennsylvania M. J. 40: 835-837 (July) 1931.

mal blood pressure early in pregnancy. Ninety-seven determinations were made for the pregnant women. Three cases occurred in the first trimester; thirty in the second and sixty-four in the third. Twelve of the patients were on a high protein diet, and forty-two were on the regular diet. Eight had definite toxemia.

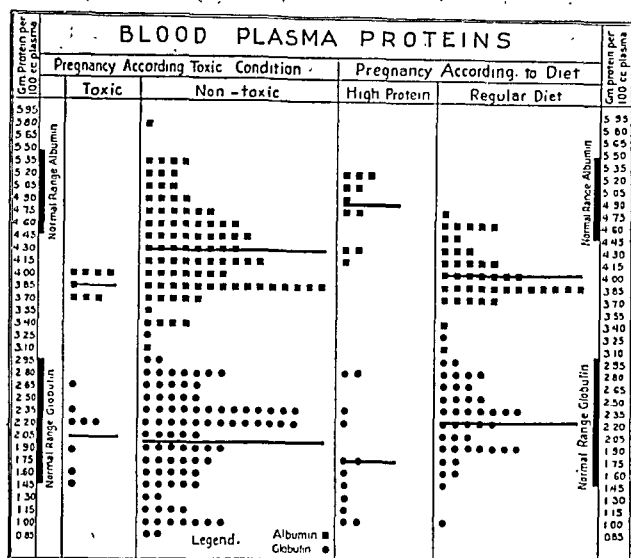


Chart 2.—Plasma albumin and globulin concentrations for the pregnant women in relation to (1) toxic condition, (2) nontoxic condition, (3) high protein diet and (4) regular diet.

The normal values, according to the literature, are from 4.5 to 5.5 Gm. per hundred cubic centimeters of plasma for albumin and from 1.5 to 3 Gm. per hundred cubic centimeters of plasma for globulin.

The class values for the various groups were scaled to 0.15 divisions; for example, all values for globulin in the class 1.6 Gm. were 1.52 Gm. or more and less than 1.67 Gm.

The average, or mean, for the nonpregnant women was  $4.90 \pm 0.06$  Gm. for the albumin and  $1.88 \pm 0.06$  Gm. for the globulin, showing low values but within the normal range. Most of these patients were of the low economic group, who eat only small amounts of meat and milk and few eggs.

The pregnant women as a whole showed a lower mean value than the nonpregnant women, the mean for albumin being  $4.27 \pm 0.04$  Gm. and for globulin  $2.01 \pm 0.04$  Gm. The mean values for albumin for the first trimester,  $4.70 \pm 0.18$  Gm., were higher than those for the pregnant women as a group but lower than the mean for the nonpregnant women. The number of women in the first trimester was very small because most clinic patients do not come to the clinic before the fourth month. The mean value for globulin for this group was lower than that for all the pregnant women, being  $1.5 \pm 0.14$  Gm. There was very little difference in the mean values for albumin for the second and third trimesters, but the values for both were lower than for the first trimester or the nonpregnant women, being  $4.18 \pm 0.06$  Gm. and  $4.30 \pm 0.05$  Gm., respectively. The mean values for globulin for the second and third trimesters were  $2.11 \pm 0.06$  Gm. and  $1.99 \pm 0.05$  Gm., respectively.

The values for patients with toxemia showed a definite lowering of the albumin to  $3.87 \pm 0.03$  Gm. but a rise in globulin to  $2.07 \pm 0.09$  Gm. The change in albumin is in agreement with the experience of Strauss and others. The rise in globulin is a new observation

and should be verified. It may be in the nature of a compensatory rise. For the patients receiving a high protein diet, the values were very close to those for the controls; namely,  $4.90 \pm 0.09$  Gm. for albumin and  $1.76 \pm 0.12$  Gm. for globulin, the globulin average being slightly lower than that for the control patients. None of the patients receiving a high protein diet showed any evidence of toxemia, and subjectively they felt very well. Their urine and their blood pressure remained normal. The values for the patients receiving the regular diet were lower than those for the nonpregnant women, being  $4.04 \pm 0.04$  Gm. for albumin and  $2.25 \pm 0.05$  Gm. for globulin.

Chart 3 shows four representative cases. The first two patients had normal blood pressure and weight gain with no toxic symptoms:

CASE 1.—D. E., a Negro primipara aged 17, seven months pregnant, was told to forget her pregnancy and to eat as she pleased. This was her first pregnancy, and she had had no dietary instructions previously. The plasma albumin content dropped gradually from 4.13 to 3.84 Gm. as the globulin rose from 2.12 to 2.28 Gm.

CASE 2.—E. H., a Negro tertipara aged 21, eight months pregnant, was told to follow her regular diet but after two weeks admitted that she had been adding eggs and milk because they made her feel better. We insisted that she refrain from taking the proteins, and on the subsequent two visits she assured us that she was eating as she did when not pregnant.

The next two cases illustrate the effect of the change in diet:

CASE 3.—R. S., a Negro sextipara aged 32, six months pregnant, was changed from her regular diet to one high in protein, containing from 70 to 80 Gm. a day. The albumin rose from 3.98 to 5.07 Gm. and the globulin fell from 2.79

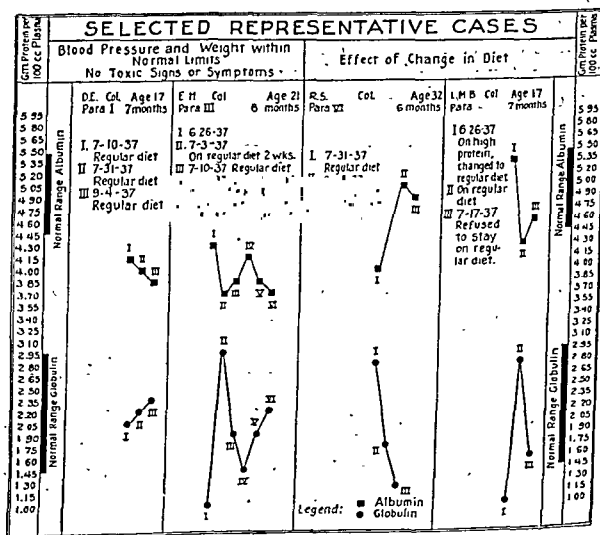


Chart 3.—Plasma albumin and globulin concentrations for four patients, showing the effect of regular diets and a change in diet.

to 1.71 Gm. She had had no complaints or symptoms previous to the change in diet. The next month there was a drop in the albumin and globulin.

CASE 4.—L. M. B., a Negro primipara aged 17, seven months pregnant, had been receiving a high protein diet for two or three weeks and was told to return to her old way of eating. One week later the albumin had fallen from 5.30 to 4.23 Gm. and the globulin had risen from 0.83 to 2.37 Gm. She refused to remain on her old diet and had been increasing the amount of milk and eggs. At this time the albumin had risen to 4.67 Gm. and the globulin had fallen to 1.65 Gm.

As has previously been stated, the rise in the globulin with the lowering of the albumin in the plasma is apparently a new observation and should be verified.

## COMMENT

Rosenstein<sup>7</sup> more than sixty years ago advanced the theory that cerebral edema caused eclampsia and that edema was due to the effusion of serum from the "too watery" blood into the cerebral tissues. Thirteen years later Charpentier<sup>8</sup> agreed with others that a diminished amount of albumin in the blood was a predisposing cause in the production of eclampsia. Wieloch<sup>9</sup> in 1925 reported the universal occurrence of water retention in his cases of toxemia of pregnancy. Bingham<sup>10</sup> found that toxemia developed in his patients only with excessive gain in weight. The cause of edema in toxemia has been attributed to many things: excessive production of the pituitary antidiuretic hormone,<sup>11</sup> primary kidney disease,<sup>12</sup> instability of the plasma colloids,<sup>13</sup> pressure on the ureter of the enlarged uterus<sup>14</sup> and excess of sodium chloride.<sup>15</sup> In 1937 Strauss<sup>16</sup> observed that patients with hypoproteinemia had a significant gain in weight, with visible edema, rises in blood pressure and in a few cases albuminuria, when sodium was administered as chloride or bicarbonate.

Strauss<sup>17</sup> found that in cases of toxemia with or without convulsions the plasma albumin is lower than that of pregnant women receiving an average diet. The average level of the globulin in his cases was not lower than that of pregnant women receiving an average or low protein diet. The average level of plasma albumin for all our pregnant women was higher than that of his patients. Those of our patients who had signs of toxemia had an average level higher than that of Strauss's patients. The average level of globulin in our cases was lower than in Strauss's cases except in those of toxemia, in which it was slightly higher.

As yet there does not seem to be a clearly defined cause for the lowering of the plasma proteins during pregnancy. It has long been recognized that the fetus is a parasite, drawing from the maternal organism the necessary nourishment for its development and growth regardless of the depletion of the mother's tissues. It is known that calcium will be removed from the body when the blood does not contain a sufficient amount to supply the needs of the fetus. Proteins are essential for growth and repair of body tissue in the adult and certainly are required in considerable amounts by the fetus and its membranes. It would seem necessary for the mother to supply by her diet sufficient proteins to maintain her own growth and repair and supply the needs of the fetus if she is not to deplete her own tissues. That there is a definite decrease in the plasma protein can be seen by our figures, which corroborate those of other authors. As has already been noted, there is considerable variation in the amount of protein which is considered to be adequate in normal pregnancy and in toxemias. The League of Nations Technical

Commission of the Health Committee on Nutrition<sup>18</sup> recommended for normal pregnant women from 1.5 to 2 Gm. of protein daily for each kilogram of body weight, which would mean from 70 to 130 Gm. a day for the woman of 150 pounds (68 Kg.); this is a little higher than the intake advised by Harden<sup>5</sup> in cases of toxemia but considerably less than that used by Strauss<sup>17</sup> in his cases. The revised report of this committee<sup>19</sup> stated, in listing the protein requirements of pregnant women, that "some animal protein is essential and in the growing period should form a large proportion of the total protein." The daily amount of protein after the fourth month of pregnancy recommended in this report is 1.5 Gm. per kilogram of body weight.

## SUMMARY

1. In pregnant women the blood plasma albumin is decreased below the level found in nonpregnant women.
2. Toxemias of pregnancy uncomplicated by organic disease are associated with a significant decrease of plasma albumin and a questionable increase of the globulin. The increase of the globulin needs further investigation.
3. Pregnancy without signs of toxemia and a diet deficient in protein cause a decrease in plasma albumin.
4. An increased intake of protein in cases of mild toxemia causes an alleviation of objective and subjective symptoms and signs and is well tolerated by the patient.

## ABSTRACT OF DISCUSSION

DR. THOMAS ADDIS, San Francisco: The authors of the paper are conservative when they say that they do not think a "clearly defined cause for the lowering of the plasma proteins in pregnancy" has been demonstrated. Their own observations as well as other clinical and experimental data show that the principal and necessary cause is a protein intake that is too low relatively to the greatly increased need for protein during pregnancy. My associates and I have completed experiments in which we compared the total body protein and organ protein of two groups of rats of identical original body weights, one a control group of female rats and the other a group in late pregnancy. We found that in all parts of the body the concentration of protein was less in the pregnant than in the control group and that the greatest change occurred in the blood serum, where the protein content fell from 6.7 per cent to 5.4 per cent. The cause of this change is given by the observation that the pregnant group were obliged to allocate 10 per cent of all the protein in their bodies for the construction of the embryos and uterus and had to use in addition 5 per cent of their total protein for new construction that the pregnancy made necessary. The mothers did their best to meet this requirement by eating more food. But the protein concentration was too low. Even though they ate 50 per cent more than the controls they could not get enough protein. Their gastrointestinal capacity was the limiting factor. As a consequence, they fell into a protein deficit, and the debt was paid at the expense of the mothers for the benefit of the babies. Drs. Dodge and Frost will agree that the need for more protein in the diet continues beyond pregnancy and throughout lactation. We are finding that in rats a diet that is entirely adequate for growth fails to maintain the usual protein content of the mothers' organs and tissues during lactation. The practical importance of these observations of Drs. Dodge and Frost is unquestioned. They give direct evidence that diets sufficient under ordinary conditions for maintenance are grossly inadequate in protein concentration during pregnancy. If we are to exclude the gastrointestinal tract as a limiting factor, it is not enough to give plenty of all sorts of food. We must see that pregnant and lactating women are given food with a high proportion of meat, fish, milk and eggs. From an economic point

7. Rosenstein, S. S.: *Traité pratique des maladies des reins*, Paris, Adreïn Delahaye, 1874.

8. Charpentier, L. A. A.: *A Practical Treatise on Obstetrics*, New York, William Wood & Co., 1887, vol. 2.

9. Wieloch, J.: *Arch. f. Gynäk.* **123**: 337, 1925.

10. Bingham, A. W.: *Am. J. Obst. & Gynec.* **23**: 38 (Jan.) 1932.

11. Anselmino, K. J., and Hoffman, Friedrich: *Arch. f. Gynäk.* **147**: 652 (Dec.) 1931.

12. FitzGibbon, G.: *J. Obst. & Gynec. Brit. Emp.* **29**: 402, 1922.

13. Eufinger, H.: *Klin. Wchnschr.* **7**: 492 (March 11) 1928.

14. Poten, W.: *Monatschr. f. Geburtsh. u. Gynäk.* **69**: 25 (April) 1925.

15. de Snoo, K.: *Am. J. Obst. & Gynec.* **34**: 911 (Dec.) 1937.

16. Strauss, M. B.: *Am. J. M. Sc.* **194**: 772-783 (Dec.) 1937.

17. Strauss, M. B.: *Am. J. M. Sc.* **190**: 811 (Dec.) 1935.

18. League of Nations Technical Commission of the Health Committee in Nutrition, 1935.

19. League of Nations Technical Commission of the Health Committee: *The Problem of Nutrition*, 1936, vol. 2, p. 15.

of view this may sometimes be difficult, but that it is a strict requirement from the point of view of physiology and of medicine there can be no doubt.

DR. BOYD HARDEN, Burlington, N. C.: I wish to make one point concerning nitrogen deficits in the toxemias of pregnancy. The discussion is based on the premise that there is a physiologic optimum beyond which the administration of protein may accomplish no benefit; there is a pathologic minimum below

### Study of Nineteen Preeclamptic and Nineteen Eclamptic Patients

#### PREECLAMPTIC PATIENTS

Average Height	Average Weight	Average Age	Average Intake in Grams		
			Protein	Fat	Carbohydrate
155.49 cm.	80.4 Kg.	33 years	82	61.1	218
On the Du Bois Chart:					
155.49 cm. meets 80.4 Kg. at 1.8 square meters.					
At 33 years of age the female requires 36.2 calories per square meter of surface area per hour.					
1.8 square meters $\times$ 36.2 calories $\times$ 24 hrs. = 1,563.84.					
Dietary values:					
Protein .....	82.0 Gm.	$\times$ 4 calories per gram			328.00 calories
Fat .....	61.1 Gm.	$\times$ 9 calories per gram			549.90 calories
Carbohydrate .....	218.0 Gm.	$\times$ 4 calories per gram			872.00 calories
Administered in diet.....					1,749.90 calories

Urine:					
Average total nitrogen.....	7.60	Protein equivalent..	47.50 Gm.		
Average nonprotein nitrogen	6.68	Protein equivalent..	41.75 Gm.		
		Protein loss.....	5.75 Gm.		

Feces:					
Average total nitrogen.....	2.20	Protein equivalent..	13.75 Gm.		
Analysis:					
Protein administered and consumed.....	82.00 Gm.				
Protein metabolized and lost.....	61.25 Gm.				
Protein stored .....	20.75 Gm.				

This protein storage appears in the presence of a starvation level of excretory products of nitrogen in urine. The actual level of excretory products of nitrogenous metabolism was 0.52 Gm. per kilogram of body weight.

#### ECLAMPTIC PATIENTS

Average Height	Average Weight	Average Age	Average Intake in Grams		
			Protein	Fat	Carbohydrate
154.1 cm.	80 Kg.	26.3 years	69.4	61	209
On the Du Bois Chart:					
154.1 cm. meets 80 Kg. at 1.8 square meters.					
At 26.3 years of age the female requires 36.6 calories per square meter of surface area per hour.					
1.8 square meters $\times$ 36.6 calories $\times$ 24 hours = 1581.12 calories as the basic caloric requirement of the mother.					
Dietary values:					
Protein .....	69.4 Gm.	$\times$ 4 calories per gram			277.60 calories
Fat .....	61.0 Gm.	$\times$ 9 calories per gram			549.00 calories
Carbohydrate .....	209.0 Gm.	$\times$ 4 calories per gram			836.00 calories
Administered and consumed in diet.....					1,662.60 calories

Urine:					
Average total nitrogen.....	7.42	Protein equivalent..	46.37 Gm.		
Average nonprotein nitrogen	6.08	Protein equivalent..	38.00 Gm.		
		Protein loss.....	8.37 Gm.		

Feces:					
Average total nitrogen.....	3.40	Protein equivalent..	21.25 Gm.		

Analysis:					
Proteins administered and consumed.....	69.4 Gm.				
Proteins metabolized and lost.....	67.6 Gm.				
Protein stored .....	1.8 Gm.				

This protein storage appears in the presence of a starvation level of excretory products of nitrogen in urine. The actual level of excretory products of nitrogenous metabolism was 0.425 Gm. per kilogram of body weight.

which the restriction of this vital constitutional element must result in manifestations of deficit. Further, in severe hepatic disease the selection of proteins essential in growth and development is necessary to the pattern needs of the fetus and the storage demands of the maternal host. This study represents a period of seven years during which 739 consecutive admissions with late gestational toxemia and eclampsia were studied under a regimen designated as protein stabilization. Nineteen patients with typical manifestations in preeclampsia and a like number with eclampsia have been selected for this discussion. During the seven years, no patient with well defined preeclampsia developed eclampsia under the regimen of protein stabilization, while the incidence of eclampsia in the community remained the same

that it was before the institution of this regimen. The application of the usual methods of antepartum care and the compensation of nitrogen deficits have proved life saving in our hands in preeclampsia and eclampsia.

DR. EVA F. DODGE, Montgomery, Ala.: We felt that we should have a larger number of determinations before drawing final conclusions. The few patients who were given the increased protein diet, particularly the eggs, milk and cheese which we found to be within the reach of our rural clinic patients despite their low economic status, were apparently helped by this diet. A pregnant girl of 13 years who was not included in the case reports had a high blood pressure without any other marked toxic symptoms. The blood pressure did not come down with an adequate protein diet. Labor was induced because of the continued high blood pressure. As her blood pressure was about 200 systolic and 110 diastolic six months after delivery we felt that it was not a protein deficiency which was responsible for the high blood pressure. We feel that the whole egg may have something to do with this problem and are now advocating the use of the whole egg instead of just the whites of the eggs. We realize that during lactation the mother needs protein, but our work was entirely with the antepartum group and we did not go into the postpartum problem.

### RADIOSENSITIVITY OF MALIGNANT NEOPLASMS OF THE UTERINE CERVIX

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AND

ROBERT E. FRICKE, M.D.

ROCHESTER, MINN.

Carcinoma of the uterine cervix is radiosensitive. Radiosensitivity means sensitive to radiant energy; specifically it is used to describe certain tumors that are susceptible of being injured or destroyed by radium and roentgen rays. This fact was soon learned by the early workers in the field of radium therapeutics. The disease was among the first malignant tumors observed to be amenable to the rays of radium.

The radiosensitivity of the lesion under consideration is relative, since the degree of injurability or destroyability is dependent on many factors. Apparently some of these factors can be evaluated, at least in a measure or in a limited degree. Ewing said: "The general condition of the patient determines the result of radiation, regardless of nearly all other factors. In fresh subjects in good general health, without anemia or cachexia, the results of radiation are usually prompt and definite, whereas in anemic and cachectic subjects with poor circulation, tumors may fail entirely to respond." Some of these factors can be recognized grossly while others are recognized microscopically. The former lend themselves rather well to recognition and discussion while the latter may be studied only by examination of material which is removed at operation or for biopsy, and by postmortem examination of specimens by skilled pathologists. As a rule, the supply of tissue for microscopic study is very limited, especially when one considers that the response to treatment requires days or weeks and that repeated removal of tissue is necessary. During a course of treatment the removal of representative tissue from time to time for microscopic study and for the evaluation of the results of treatment is considered dangerous or inadvisable.

From the Section on Therapeutic Radiology, the Mayo Clinic. Read before the Section on Radiology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

The capacity of a given malignant lesion of the cervix to respond to irradiation can be determined by frequent observations during the course of treatment, and the duration of this response can be in a measure determined by the number of three year or five year cures in a group of cases. The data presented in this paper were obtained from our daily experience and from the three year results obtained in a group of 1,491 cases in which treatment was given in the years 1915 to 1929 inclusive. As a rule the diagnosis can be made from the chief complaint, history, bimanual pelvic examination and inspection of the vaginal cavity, preferably with the patient in the knee-chest position. The removal of small bits of tissue for microscopic study is of value in confirming the clinical diagnosis and in determining the grade of malignancy. Material for biopsy can be obtained with but little, if any, risk. The diagnosis was confirmed by histologic examination in 947 cases; 872 of the 947 patients were traced after they left the clinic; 372, or 42.7 per cent of these patients, lived three or more years after the treatment. In the entire series of 1,371 traced patients 473, or 34.5 per cent, lived three or more years after the treatment. In the early years covered by this study a biopsy was an elective procedure, but at the present time it is performed as a matter of routine. The routine performance of biopsy has advanced our knowledge of this dreaded disease. Malignant neoplasms of the uterine cervix consist chiefly of squamous cell epitheliomas, which have a dominant tendency toward the higher grades of malignancy. The remaining small group is made up of adenocarcinomas and a few mixed lesions which contain both of these malignant cellular elements. In the majority of the cases an extensive primary lesion is associated with an inflammatory or degenerative process and the therapeutic management<sup>1</sup> requires special consideration.

From the standpoint of radium therapy it is important to classify the lesions according to the extent of the primary and secondary involvement. The following classification has proved satisfactory: Stage 1 indicates that the primary lesion is limited to the uterine cervix, stage 2 indicates that the primary lesion has extended beyond the original site but the uterus is movable, stage 3 indicates that the primary lesion has extended further than in stage 2 and that the uterus is definitely fixed, stage 4 indicates a "frozen pelvis" with extensive pelvic involvement and the probable presence of local and distant metastasis. The term "modified" is used to describe the stage of involvement in cases in which some type of therapeutic procedure

had been employed before the patients came to the Section on Radium Therapy. Modified stage 1 denotes that the active lesion is rather small, while modified stage 4 denotes that a "frozen pelvis" is present.

The radium technic employed at the clinic in the treatment of carcinoma of the uterine cervix may be defined as an intensive, multiple or broken-dose method. This procedure is orderly, flexible and effective. The radium therapist should have at his disposal an assortment of applicators such as universal tubes, various needles and gold (radon) seeds. The treatment factors, that is, the amount of radium, the filtration and the distance, as a rule should remain constant, while the time of application and the interval between applications should be varied to meet the needs of the patient. Nearly all patients are placed in the knee-chest position in order to permit careful inspection and the introduction of applicators without trauma

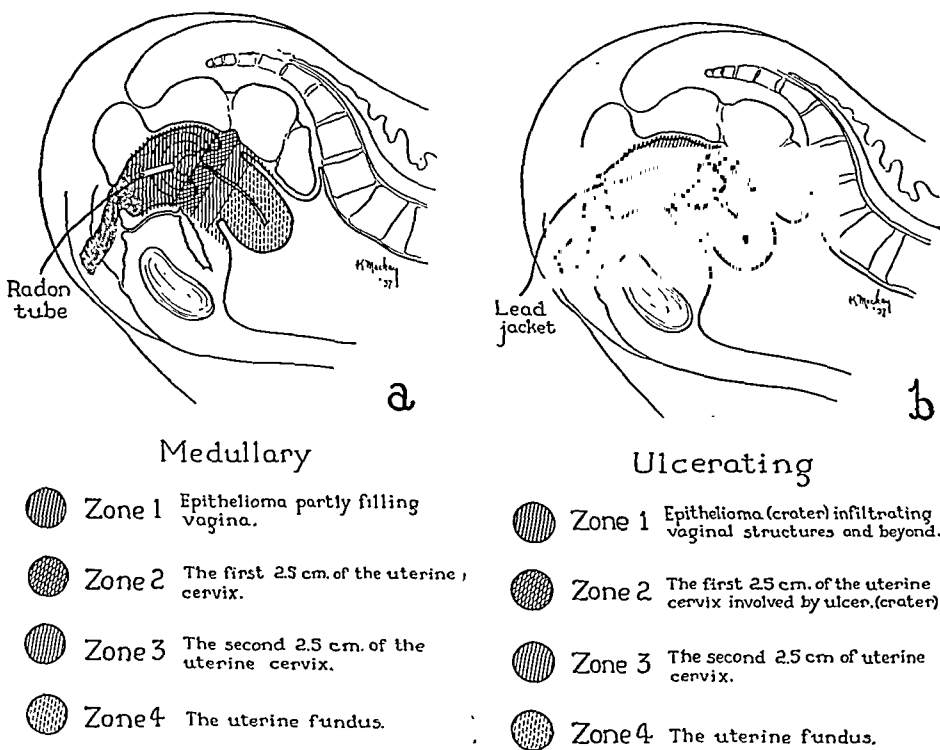


Fig. 1.—Treatment of (a) medullary type, and (b) infiltrating types of uterine carcinoma. Patient in knee-chest position and applicator in place.

(fig. 1). The intervals are necessary to determine the radiosensitivity of the treated lesion. In cases in which such complications as tumor necrosis, local cellulitis, ulceration of the vaginal walls that is indicative of potential fistulas, or pyometritis are present the intervals permit the proper institution of active measures to combat these serious, if not dangerous, conditions. In the final part of the course, the treatments are applied more rapidly. The other details are shown in figure 2, in which the probable treatment schedule for an average patient with a stage 3 involvement is outlined. The radium therapy is followed by a course of so-called high voltage roentgen therapy. The combined method of treatment was employed in 1,450 of the 1,491 cases in this series. In the remaining forty-one cases roentgen therapy was the only treatment used.

The classification of the courses of radium treatment is essential for their evaluation. In the event that the

1. Bowing, H. H., and Fricke, R. E.: Carcinoma of the Uterine Cervix: A Survey of Treatment and Results in 1,491 Cases, *Am. J. Roentgenol.* 40: 47-51 (July) 1938.



treatment is applied as outlined, together with any additional or probable reduction in the number of applicators, it is classed as complete. In some cases, owing to the character and extent of the local or pelvic involvement, only part of the outline can be carried out. In such cases the treatments are classed as limited. During the course of treatment it may become necessary to stop treatment and in this event the treatment is classed as abandoned. Table 1 shows the most significant factor in estimating the longevity of these patients; 52.9 per cent of the patients who received a complete treatment and 21.4 per cent of those who received only a limited treatment lived three or more years after treatment. This result is all the more significant because in more than 90 per cent of the 1,491 cases the involve-

the treatment may furnish an index. All treatable patients are benefited. The vaginal discharge stops, the tendency to bleed stops, and in many cases the relief of pain is prompt. The degree and the duration of this improvement depend on the extent of malignant involvement and the adequacy with which treatment can be applied.

The patient with stage 1 and modified stage 1 involvement has the best chance of living three or more years after treatment, while the patient who has stage 4 and modified stage 4 involvement has the least chance of living three or more years after treatment. In brief, all treatable patients have a chance of living three or more years after treatment (table 2). An evaluation of these results indicates that the extent of involvement

plays a major role in the determination of the longevity of the patient after treatment.

Grossly, there are two types of carcinoma of the uterine cervix; these usually are designated as (1) medullary carcinoma and (2) infiltrating or ulcerating carcinoma. The latter type predominates and is more radioresistant than is the former. The grade of malignancy cannot be determined from the gross characteristics of the lesion. However, the gross appearance of the lesion does determine the selection of the type of treatment to be employed in a given case. In other words, the estimation of the grade of malignancy is of but little if any assistance to the radium therapist in determining the treatment to be employed. This statement must be made with a certain amount of reservation because a low grade of malignancy seldom is encountered in cases of carcinoma of the uterine cervix and when it is en-

countered the neoplasm usually is an adenocarcinoma. It is doubtful whether a squamous cell epithelioma, grade 1, was ever encountered.<sup>2</sup> In other words, our experience centers around the predominating grade 3 and grade 4 lesions. It is evident that if a number of patients who have carcinoma of the cervix are treated individually, irrespective of the grade of malignancy, and if the patients later are grouped according to the grade of malignancy, there will be little difference in the number of three year cures obtained in the various groups. The data in table 3 are submitted to substantiate this statement. Forty per cent of the patients with lesions of grade 1 and 41.1 per cent with lesions of grade 4 lived three or more years after treatment.

Briefly, it seems possible to obtain the same radiotherapeutic result in the treatment of this disease regardless of the grade of malignancy, but one must

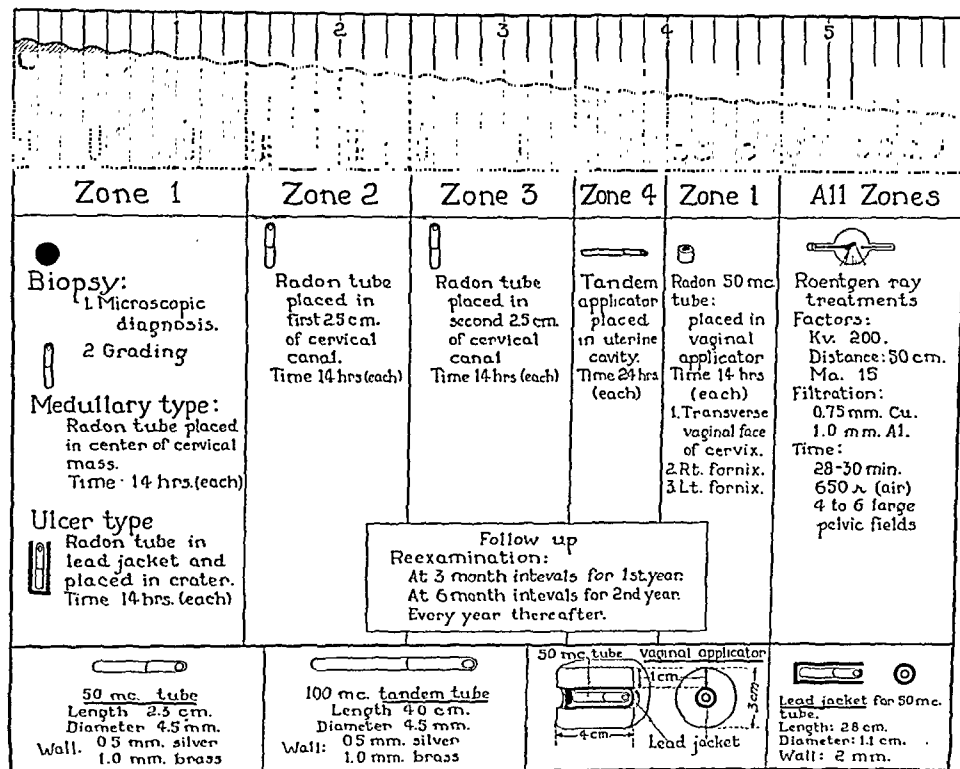


Fig. 2.—Schedule of radium treatment for the average stage 3 involvement in a case of carcinoma of the uterine cervix. Each of the Arabic numerals across the top of the drawing indicates the end of one week of treatment. The vertical line which is intercepted by each Arabic numeral, and every other similar vertical line, indicates the end of one day. The wavy line which descends from left to right indicates the decreasing infiltration and the general improvement of the patient's condition as treatment progresses. Directions for a complete treatment can be obtained by reading the chart from left to right.

ment was extensive (stages 3 and 4, table 2). The large number of patients who received limited treatments can be explained as follows. They were treated in the early years covered by this study and when compared with the patients treated in the later years of this study their therapeutic management was considered to be a limited treatment. Of the patients whose treatment was abandoned 30.3 per cent lived three years or more after the treatment (table 1). Much depends on the amount of treatment applied before it is necessary to stop the applications. The analysis of this group is fascinating; many of the patients who lived three or more years after the treatment received a very limited treatment. The associated complications may have been a deciding factor in the response to radium therapy.

We have no statistical data to confirm the statements made about the immediate or initial result. However, the patients who lived three or more years after

2. Broders, A. C.: Personal communication to the authors.

remember that the cases in which the grade of malignancy was low were very few in number and do not warrant a statistical review or opinion. These statistical data warrant further study. We are in accord with MacCarty's statement that one is prone to accept observations too quickly and is likely to draw premature conclusions; this especially is true of microscopic grading and sensitivity.<sup>3</sup>

In order to study the influence of age on the longevity of this group of patients they were grouped according

TABLE 1.—Results According to the Type of Radium Treatment Employed

Classification of Radium Treatment	Patients Treated	Patients Traced	Patients Who Lived Three or More Years After Treatment	
			Number	Per Cent of Those Who Were Traced
Complete.....	604	563	299	52.9
Limited.....	807	739	158	21.4
Abandoned.....	39	33	10	30.3
Total.....	1,450*	1,337	467	34.9

\* This does not include forty-one cases in which roentgen therapy was used alone.

TABLE 2.—Results of Treatment of Carcinoma of the Uterine Cervix with Irradiation Alone, Based on Stage of Lesion

Stage of Lesion	Patients Treated	Patients Traced	Patients Who Lived Three or More Years After Treatment	
			Number	Per Cent of Those Who Were Traced
Stage 1.....	13	13	12	92.3
Stage 2.....	85	81	57	70.4
Stage 3.....	823	760	292	38.4
Stage 4.....	156	142	18	12.7
Modified stage 1.....	4	4	4	100.0
Modified stage 2.....	28	26	18	69.2
Modified stage 3.....	297	271	68	25.1
Modified stage 4.....	83	74	4	5.4
Total.....	1,491	1,371 (91.9%)	473	34.5

to their ages by decades (table 4). It is an accepted fact that young patients do not tolerate malignant disease as well as do older patients. In other words, the young patient with malignant disease has a poorer prognosis than does an older patient. The data in table 4 substantiate this statement. The number of three year cures of patients treated before the age of 49 years was less than it was of patients treated after the age of 49 years. Patients who were in the fourth and fifth decades of life when radiation therapy was started showed little difference in the percentage of three year cures; however, this statement does not hold true if the patients who were in the third decade of life are included. This may indicate that if it is possible to employ individual treatment for patients in the fourth and fifth decades of life the percentage of three year cures will be approximately the same in the two groups. The percentage of three year cures was increased for patients who were beyond the age of 49 years. It seems probable that age may influence the degree of radiosensitivity but it is possible that the primary lesion responds equally regardless of the age of the patient. However, if metastasis to distant organs occurs before the age of 49 years it may be the factor that reduces the number of three year cures. We do not have data that confirm or disprove this statement.

3. MacCarty, W. C.: Microscopic Grading of Tumors, Its Interpretation, Limitations and Relation to Radiosensitivity, *Am. J. Roentgenol.* 37: 365-367 (March) 1937.

A second significant factor occurs in the data contained in table 5. The patients treated early in our experience received a limited radium treatment, for example about 2,000 mg. hours, which may be considered a surface treatment. This was supplemented with the so-called low voltage roentgen therapy and the initial result was favorable; when the patients were seen after an interval of a few weeks, or months, however, activity was demonstrable. As a further palliative procedure the initial treatment was repeated. Many patients received several such treatments but, as a rule, malignant activity was demonstrated on subsequent visits. A careful review of these cases was encouraging but it was evident that the technic was deficient as it did not provide proper distribution of the therapeutic rays of radium, and the initial total dose was too small. For these reasons our present technic was evolved; this accounts in a great measure for the difference in results shown in table 5. Today an initial complete treatment is never repeated and the result is superior when compared with our early results. Of the patients treated between 1915 and 1919 inclusive 14.4 per cent and of the ones treated between 1925 and 1929 inclusive 42.7 per cent lived three or more years after treatment. The radium technic employed today began

TABLE 3.—Results of Treatment of Carcinoma of the Uterine Cervix with Radiation Therapy, Based on the Grade of Malignant Change

Grade of Malignancy	Patients Treated	Patients Traced	Patients Who Lived Three or More Years After Treatment	
			Number	Per Cent of Those Who Were Traced
Grade 1.....	5	5	2	20.0
Grade 2.....	135	125	56	44.8
Grade 3.....	407	372	161	43.3
Grade 4.....	336	311	123	41.1
Biopsy performed but malignancy was not graded.....	64	59	25	42.4
No biopsy performed..	544	499	101	20.2
Total.....	1,491	1,371 (91.9%)	473	34.5

TABLE 4.—Results Obtained in the Treatment of Carcinoma of the Uterine Cervix with Irradiation, Based on Age of Patients

Age of Patient, Years	Patients Treated	Patients Traced	Patients Who Lived Three or More Years After Treatment	
			Number	Per Cent of Those Who Were Traced
20 to 29.....	28	25	5	20.0
30 to 39.....	284	266	78	29.3
40 to 49.....	496	458	145	31.6
50 to 59.....	452	416	160	38.5
60 to 69.....	208	185	78	42.2
70 to 79.....	22	20	6	30.0
80 to 89.....	1	1	1	100.0
Total.....	1,491	1,371 (91.9%)	473	34.5

to take form in or about the year 1920. We were favorably impressed with the early results, which encouraged us to persevere and perfect our present plan of treatment.

The hospital mortality was calculated on the basis of the type of treatment applied (table 6). There were 604 complete treatments with one death, a mortality of 0.2 per cent. There were 807 limited treat-



ments with five deaths, a mortality of 0.6 per cent. Every endeavor is made at the time the patient is first seen to select the best type of treatment to meet the therapeutic needs. In other words, every effort is made to avoid, if possible, abandoning treatments. When one considers the numerous applications made throughout the years, the risk attached to a single treatment must be very small; however, the cumulative effect cannot be ruled out. A limited treatment indicates an extensive pelvic involvement and poor general health; it naturally indicates that the risk of treatment would be increased. The hospital mortality in the cases in which the treatment was abandoned was 15.4 per cent. The hospital mortality in the entire series was 0.8 per cent.

## SUMMARY

The radiosensitivity of carcinoma of the uterine cervix is a relative feature and its significance must be fully appreciated in the therapeutic management of

TABLE 5.—Results of Radiation Therapy According to Five Year Periods in Which Treatment Was Given

Five Year Period in Which Treatment Was Given	Patients Treated	Patients Traced	Patients Who Lived Three or More Years After Treatment	
			Number	Per Cent of Those Who Were Traced
1915 to 1919, Inclusive..	288	264	38	14.4
1920 to 1924, Inclusive..	556	522	185	35.4
1925 to 1929, Inclusive..	647	585	250	42.7
Total.....	1,491	1,371 (91.9%)	473	34.5

TABLE 6.—Hospital Mortality Based on the Classification of Radium Treatment Applied

Type of Treatment	Patients	Hospital Deaths	
		Number	Per Cent of Those Who Were Traced
Radium:			
Complete.....	604	1	0.2
Limited.....	807	5	0.6
Abandoned.....	39	6	15.4
Roentgen therapy alone.....	41	0	
Total.....	1,491	12	0.8

\* Included in table to account for full total of cases. Not accepted for radium treatment.

this disease. If carcinoma of the uterine cervix and the associated inflammatory and degenerative process are effectively treated with radium and supportive measures, the result of treatment is prompt and its duration is evidenced by the percentage of three year cures. An attempt has been made to use the late results as an index of the radiosensitivity of the lesion. Patients possess many potentialities which affect the results of irradiation. The immediate result is influenced definitely by the extent of the malignant process. It is evident that the age and general health of the patient, the equipment and the skill and experience of the therapeutic radiologist have a definite influence on the late result. The best results are obtained in cases in which the treatment is classed as complete at the first session. However, subsequent treatment may produce relief that will last for years. The initial course of radium treatment requiring two, three or more weeks is necessary before one can evaluate the immediate results and determine the radiosensitivity of the lesion. An interval

of three months should elapse before one attempts to evaluate the late results. We fully appreciate the limitations of statistical data; however, the data in this paper are supported by our clinical experience.

## ABSTRACT OF DISCUSSION

DR. WILLIAM P. HEALY, New York: About 80 per cent of cancers of the cervix histologically are radiosensitive. Twenty per cent are in the adult group of cancer cells which are relatively radioresistant, but even those cases respond to irradiation because it is only a relative degree of resistance. It is for this reason that cancer of the cervix has gone out of the surgical group into the radiation field of therapy. Rarely is a case of cancer of the cervix encountered in which there is a limited degree of response to irradiation, but occasionally one will meet a case in which improvement occurs for a period of several weeks and the disease is still limited to the cervix and must be grouped as a favorable case clinically, and yet one finds that the cancer does not disappear under irradiation. That patient is incurable under any form of treatment. In this rare instance one is justified in doing a simple, complete hysterectomy, and while the patient lives, which will probably be two or three years, she will remain free from local evidence of cancer. Since all these patients have come for radiation therapy, the degree of radiosensitivity in the individual case is purely of academic interest. One makes a biopsy because one must have a histologic diagnosis in the case, but one is going to treat her with radiation therapy regardless of whether the cancer is of grade 1 or grade 2 and regardless of whether it is a squamous carcinoma or an adenocarcinoma. All cancers do better with radiation therapy in average or expert hands than with surgery. The important item is early diagnosis. If one recognizes these cases early, one has an opportunity of curing 60 per cent of the early group. At the Memorial Hospital we have had 3,500 cases of cancer of the cervix uteri, and we have been impressed by the advantages of giving x-ray therapy with the high voltage x-ray apparatus, 200 kilovolts, before radium is used. It is unfortunate that the authors used only a three year survival classification. That is much too short and is of only academic value, because for cures one must have at least a five year limit. An untreated patient with cancer of the cervix may live two years.

DR. HENRY L. SCHMITZ, Chicago: The paper of Drs. Bowing and Fricke concerns the prognosis and course of the disease in relation to the extent of the growth and the general constitutional condition. The study of the clinical extent of the growth called by the writers stages 1, 2, 3 and 4, either modified or unmodified, would be facilitated if the clinics would agree on the same definitions for each stage. It would then be possible to evaluate the end results of the various forms of treatment of carcinoma of the cervix. The widest differences are found in the definitions of clinical groups 1, 2 and 3. The difference between clinical group 1 and clinical group 2 cases is mobility of the uterus. It is normal in the former if one attaches a forceps to the uterus and it can be displaced down to the entrance of the vagina without causing the patient any distress. In clinical group 2 the uterus is limited in mobility, though movable, and it cannot be displaced downward unless one uses an appreciable pull. Limited mobility may be due to either an extension of the carcinoma or an inflammatory reaction in the pericervical tissues. It is clear that a patient with an inflammatory loss of mobility of tissue will do better than one with a carcinomatous invasion of the paracervicum. The clinical group 3 case is characterized by an invasion of either one or both parametria yet mobility of the entire mass is still present. There should be made a distinction between fixation and limited mobility of the tumor. As soon as the carcinoma becomes fixed, a clinical group 4 carcinoma is present. Presence of local or distant metastases, or invasion of adjacent organs as bladder, vagina or rectum in the absence of fixation, also stamp such a cancer as belonging to clinical group 4. Such a clinical grouping of the extent

of the growth is very important for the selection of the indicated form of treatment and for the study of the good end results. I do not wish to add to these definitions, as the proper grouping alone will enable one to select the treatment and to prognosticate the results.

DR. HENRY ULLMANN, Santa Barbara, Calif.: In the question of clinical stages 1 and 2—and Dr. Schmitz brought up the question of inflammatory reaction—I again want to emphasize, and trust that it will be brought out in the closing discussion again, that quite a number of patients whom I have seen that I would class as a 2, perhaps an early 2 because of a limited mobility, within a few days after a light course of roentgen treatment has been begun, had complete mobility and palpable induration of the immediate part of the broad ligaments. So that a clinical type 2, at first examination, becomes a clinical type 1 after some irradiation. I feel that perhaps we should add to this that a true class 2, type 2, in order to keep our statistics clear, must remain somewhat limited in mobility after a moderate dose of roentgen rays, because I do not believe that this dose will bring back the mobility so promptly unless it is due to inflammation and not to cancer.

DR. HARRY H. BOWING, Rochester, Minn.: Concerning Dr. Healy's discussion a misunderstanding has occurred, as no attempt was made to report the five year results. I did select the three year results obtained in the group of 1,491 cases for comparison to illustrate a few of the many factors that influence radiosensitivity. Briefly, the data on the 1,491 cases were arranged in tables to show the results according to the age of the patient, grade of malignancy (Broders), stage of involvement, the year of the treatment and the type of radium treatment. It is logical to assume that initial or early response to treatment of the primary lesion or, in other words, the radiosensitivity of the lesion, should also be reflected in the three year cures and that it should be possible to measure the duration of this response by an analysis of the three year cures. Naturally, the outstanding single factor governing the early and late results is the stage of the lesion at the time of treatment. In the cases in which the lesion was grade 1, 92.3 per cent of the patients lived three years, but in the cases in which the lesion was grade 4, only 12.7 per cent of the patients lived three years. There was a marked difference in the late result when the calendar year of treatment was tabulated. The technic of radium therapy has improved with the passing of the years. Of the patients treated in the early years of our experience 14.4 per cent lived three years, but of the patients treated in the last five years of this study 42.7 per cent lived three years. Evidently the improvement in technic favored or enhanced radiosensitivity. Adequate radium therapy is not possible in all cases, and as a result patients do not all obtain the same response. In this study 565 traced patients received a complete radium treatment and 52.9 per cent of these patients lived three years. Only a limited radium treatment was possible in 739 of the cases in which the patients could be traced; 21.4 per cent of the patients lived three years. Evidently the adequacy of treatment influences the radiosensitivity. The results according to age groupings are of great interest. The young and old patients are too few for analysis. Of the 458 traced patients who were between the ages of 40 and 49 years, 31.6 per cent lived three years; and of the 416 traced patients between 50 and 59 years of age 38.5 per cent lived three years. Evidently the older patients survive longer than do younger patients or radiosensitivity is influenced by the age of the patient.

**Special Institutions for the Insane.**—In summing up the movement for special institutions for the insane during the first quarter of the nineteenth century, we find such institutions being established in eight different states for the first time. Of these, six were founded as semipublic institutions by incorporated groups, and two were completely under state auspices. A ninth state, Virginia, established its second state hospital during this period.—Deutsch, Albert: *The Mentally Ill in America*, New York, Doubleday, Doran & Co., Inc., 1937.

## SODIUM CHLORIDE TOLERANCE IN CHRONIC NEPHRITIS

WITH SOME OBSERVATIONS ON THE  
POTASSIUM AND SULFATE IONS

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CHICAGO

AND

ROGER ROBINSON, M.D.

BOSTON

Work published a few years ago<sup>1</sup> on the effect of minerals on fluid balance in experimental nephrotic edema of dogs indicated that sodium entered into the formation of edema, whereas potassium acted to displace it. Further, that the chloride ion was not the active element in the storage of fluid but that it was able to facilitate the formation of edema by uniting with sodium. However, the chloride ion acted as a diuretic by drawing on stored base when administered in excess, such as ammonium chloride, and it was especially effective as a diuretic when given as potassium chloride. This led to a clinical trial of these observations which was found to be effective in many patients suffering with resistant cardiac and nephrotic edemas.<sup>2</sup> The low sodium, high potassium acid ash diet was developed, and 5 Gm. of potassium chloride was added daily for its diuretic effect and for its important assistance as a salt substitute. The past five years have further established the clinical value of this regimen in the control of such problems of edema.

Since in many cases of chronic glomerular nephritis hypertension, cardiac enlargement, gallop rhythm and edema develop late in the disease, a low sodium, high potassium neutral ash diet with potassium chloride was tried. In many instances the regimen was effective in relieving the edema, but too frequently there was a sharp aggravation of the uremic manifestations as an acidosis developed.<sup>3</sup> This led to further specific ion studies on such patients with the hope that additional information of late chronic renal disease might be obtained. Only a few of the observations made on these cases will be presented.

### METHOD

Fifteen patients who were faithful to the clinic with long-standing renal disease were sent into the research ward for a period of observation. They were placed on a diet which was found suitable to their taste and to their renal status, so that it could be completely tolerated for many weeks. The diet was then kept constant in nitrogen, phosphorus, sulfur, chloride, sodium and potassium so far as variable sources of individual foods permitted. The problem was carefully explained to the patients so that their complete cooperation was obtained except in one instance. They were kept ambulatory in the ward, sun porches and gardens, which kept them happy.

To this basic program, after a period of observation of from two to four weeks, additions of sodium

From the Bettie Soper Clements Ward of Passavant Memorial Hospital and the Department of Medicine of Northwestern University Medical School.

Read before the Section on Pharmacology and Therapeutics at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 17, 1938.

1. Barker, M. H.: *Experimental Edema: The Effects of Low Plasma-Protein Level Upon Water Balance as Related to Specific Ions: The Kidney in Health and Disease*, Philadelphia, Lea & Febiger, 1935.

2. Barker, M. H.: *Edema as Influenced by a Low Ratio of Sodium to Potassium Intake*, J. A. M. A. 98:2193 (June 18) 1932.

3. Barker, M. H.: *Some Dangers of Rapid Diuresis*, Illinois M. J. 72:313 (Oct.) 1937.

chloride, potassium chloride, sodium citrate, bicarbonate, potassium citrate, calcium gluconate or chloride, phosphoric acid or ammonium sulfate or combinations of these substances were given in amounts calculated for the individual patient. Changes in symptoms, blood pressure, edema, renal function and body chemistries were observed.

Daily weight, fluid intake and output, alternate day or biweekly blood chemical determinations were made

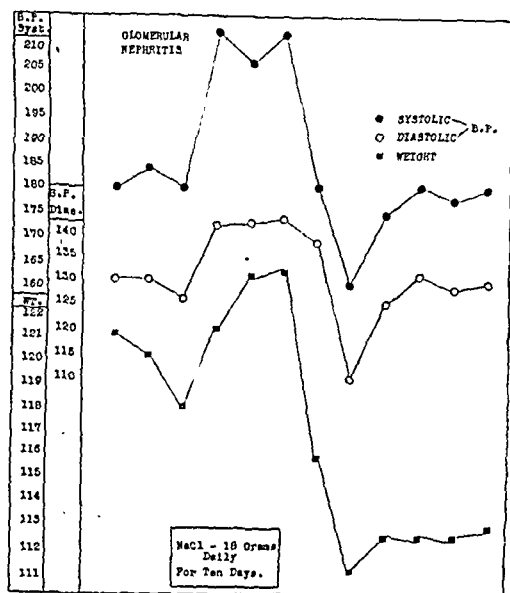


Chart 1.—The systolic and diastolic blood pressures increased sharply when sodium chloride. (the equivalent of 2 liters of physiologic solution of sodium chloride) was added to this diet otherwise constant in mineral content.

depending on the acuteness of the case. These observations consisted of the determination of sodium, potassium, calcium, chlorides, phosphates, sulfates, carbon dioxide combining power, urea, urea clearance, creatinine, serum proteins, hematocrit and fluid and blood volumes. Blood counts, phenolsulfonphthalein excretion tests, routine renal function tests, examination of the eyegrounds and chemical studies of edema fluid when present were made weekly as indicated. Blood pressures were taken twice a day.

#### RESULTS

The chief observations were those of the storage of fluid, aggravation of symptoms, elevation of blood pressure and decreased urea clearance when sodium was added to the basic diet. This was especially true of sodium chloride (chart 1). Chlorides administered as ammonium or calcium chloride or diluted hydrochloric acid frequently decreased the edema, but the associated acidosis aggravated the symptoms and depressed renal function. In certain cases presenting low blood chlorides following the forcing of fluids without a normal intake of chloride or following vomiting the chloride deficit had to be replaced, as Peters and his associates<sup>4</sup> have demonstrated. However, chlorides administered as potassium chloride usually effected a moderate or complete loss of edema and an occasional improvement of urea clearance. There was never a retention of potassium in the cases studied nor was there any evidence of potassium intoxication (chart 2). The administration of calcium orally or

intravenously did not produce sufficient changes for comment at this time. However, the addition of the acid ions of phosphate and sulfate were of special note. Both ions seemed to be effective occasionally in clearing edema and reducing blood pressure. The former, administered in its most palatable form—phosphoric acid—usually produced a hyperphosphotemia like that seen in acute nephritis or the end stage of chronic nephritis, with a resultant acidosis and aggravation of the renal state. The known seriousness of the storage of phosphorus in renal insufficiency was again clearly shown and the experiment with phosphate was soon discontinued. The sulfate, given as ammonium sulfate, had a much more satisfactory effect. Not only did the blood pressure fall and edema disappear in nine cases but urea clearance improved together with improvement of other subjective symptoms, such as loss of headache, nausea, vomiting and anorexia. Retinal edema and exudate, when present, was relieved. The latter point may be emphasized. Some observations may be more clearly indicated by reference to one of the records of a representative case.

#### REPORT OF CASE

A. B., a man aged 40, a carpenter, who had acute nephritis in 1931, continued to show urinary changes and a progressive diminution of renal function. Whenever he took salt or salt-containing foods the blood pressure would rise, the urea clearance would fall and edema would form. This state was attended by symptoms of severe headache, pounding of the heart and dyspnea; especially attacks of nocturnal dyspnea were noted whenever the blood pressure would rise over 200 mm. At the time of this study, the urine was acid, the specific gravity was from 1.010 to 1.008 and contained 2 plus albumin, from 4 to 20 red blood cells per high power field and a moderate number of hyaline and granular casts. The phenolsulfonphthalein excretion was 10 per cent and the urea clearance was 30 per cent of normal. There were moderate edema of the

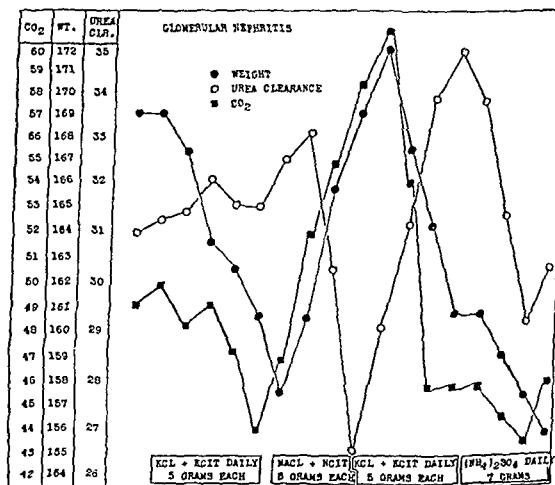


Chart 2.—The administration of the potassium ion as potassium chloride and potassium citrate was associated with a diuresis and an improvement of urea clearance while a sharp depression of the urea clearance and a rapid collection of edema followed an equal amount of sodium chloride and sodium citrate. A return to the potassium salts resulted in diuresis and an improvement of urea clearance.

face and legs, slight arteriosclerosis and cardiac enlargement. The blood pressure was 160 systolic, 120 diastolic.

The diet was kept constant, as already described. Fifteen Gm. of sodium bicarbonate was given daily for two weeks at the beginning of the study as a further check on the sodium ion (chart 3). The chief finding aside from a rapid increase in the carbon dioxide combining power was a depression of the urea clearance until buffering doses of ammonium sulfate

4. Peters, J. P.; Wakeman, A. M., and Lee, Carter: Total Acid-Base Equilibrium of Plasma in Health and Disease, *J. Clin. Investigation* 6: 517 (Feb.) 1929.

were added. A period of two weeks was allowed for a return to whatever mineral balance this patient was able to regain. At that time 15 Gm. of sodium chloride was taken orally. Very soon there was a sharp decrease in urea clearance and there was a gradual increase both of systolic and of diastolic blood pressure. Symptoms of severe headache, depression, anorexia, heart consciousness, nocturnal dyspnea and stupor gradually developed. By this time the urea clearance had fallen to 10 per cent of normal and the blood pressure had reached 220 systolic, 165 diastolic. A rather dramatic arrest of this trend, followed by an improvement of the urea clearance and a drop

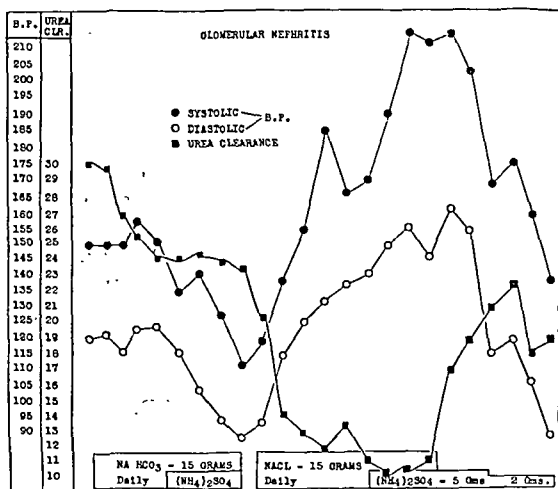


Chart 3.—Sodium bicarbonate administered to a patient with severe glomerular nephritis depressed the urea clearance slightly. When ammonium sulfate was added, the blood pressure decreased, and an arrest of the falling urea clearance was noted. An equal number of grams of sodium chloride substituted for the sodium bicarbonate caused a marked depression of the urea clearance and a sharp elevation of the blood pressure. The addition of a buffering dose of ammonium sulfate seemed to arrest the effect of the sodium chloride.

of the systolic and diastolic blood pressure, was attended by the daily addition of 5 Gm. of ammonium sulfate orally. There was a rapid improvement of all symptoms as soon as the sodium chloride was discontinued. An important sequel to this experiment was the continued symptomatic and clinical improvement attended by the continued administration of the ammonium sulfate. The patient complained of headache and a general feeling of ill-being, and there was storage of fluid and an increase of the blood pressure when the sulfate ion was discontinued. When the ammonium sulfate was resumed, not only was the patient generally improved but small amounts of salt could be taken on the food without precipitating a renal crisis as that described.

#### COMMENT

Careful clinical and metabolic studies of fifteen selected cases of advanced renal disease have shown marked elevations of blood pressure, decreases of renal function and associated symptoms in nine cases whenever sodium chloride was ingested. The many sources of sodium chloride in common foods that the salt-hungry patient will naturally select when he is on a salt-free diet renders true restriction of sodium chloride very difficult. Considerable comfort and security may be gained for the occasional patient by giving potassium chloride as a salt substitute, as previously reported. These studies suggest that when one is forced to go on a low protein diet one gives up not only protein but the phosphate and sulfate ions of the meat that play an important role in fluid balance. This factor is no doubt important in the diuretic effect of the high-protein diet frequently given the nephrotic patient. It is further shown that the chronic nephritic patient is readily upset by changes in his mineral intake, apparently because of poor mineral metabolism or clearance.

Certainly he is thrown into an acidosis or an alkalosis very easily, either extreme being dangerous. The retention of phosphorus and its effect on acid-base equilibrium with aggravation of the uremic state is emphasized. Further, the possible beneficial effects of the sulfate ion as ammonium sulfate administered in doses of from 2 to 6 Gm. daily was noteworthy in these cases. Although the buffering or neutralizing effect of sodium or some other specific function was not demonstrated in this study, its possible therapeutic value suggests further critical observation. Two patients were unable to clear sulfate readily, and an intoxication and acidosis was noted. The blood sulfates rarely increased over 3 mg., the highest being 7.8 mg. per hundred cubic centimeters. It is obvious, therefore, that although the beneficial effect of ammonium sulfate may be great, its retention must be considered. Since the low protein diet leaves the patient chiefly fruits and vegetables, which supply base in great excess, the need for nontoxic, nonthreshold neutralizing acid elements may be desirable. Ammonium sulfate has been the most helpful of the substances used. Not only is the patient who is required to take a low protein, salt-free diet kept in a better state of urea clearance, circulation and fluid balance, but the addition of ammonium sulfate may permit the taking of small amounts of salt, which renders the diet more palatable. Further, it may cover the sodium chloride, which most certainly will creep into one's food with the disastrous effects demonstrated.

700 North Michigan Avenue.

#### ABSTRACT OF DISCUSSION

DR. THOMAS ADDIS, San Francisco: This paper is definitely of an experimental nature and so I hope that when the paper is published the authors will make it clear that they are not recommending a low sodium, high potassium diet for all patients with chronic nephritis. It is safe enough for the authors to do it in certain special situations but it wouldn't be safe for the rest of us to use it in all cases. In fact, nothing could be more dangerous than such a diet for patients who are approaching the uremic level, because there one is dealing with a situation in which there is already a strong tendency to lose sodium on account of decrease in renal reabsorption of sodium; and when that is accentuated by any exceptional loss of sodium such as may be produced by vomiting, and it occurs in a patient who is already on a low sodium diet, then unquestionably conditions exist that favor acute renal failure, from which one may save the patient by actually giving him sodium. With respect to a high potassium diet I have a suspicion that in patients who are approaching the uremic level that also may be dangerous. The reason is that I have been making some observations on rats in which an experimental form of uremia had been produced by tying the vena cava. It was found that meat was very toxic to these animals; it increased the mortality. It was natural at first to suppose that this was due to some organic substance associated with the protein in the meat, but further analysis of the situation forced the conclusion that it was really the high potassium content of the meat, not any organic constituent, which was mainly responsible for the increased mortality. And that observation has been verified under altogether different conditions by Dr. Drury at the University of Southern California. Quite independently he came to exactly the same conclusion. I am therefore asking the authors to make it very clear to those who are treating the glomerular nephritis that a low sodium, high potassium diet is no general prescription and that it can be used only under known and highly specific conditions.

DR. WILLIAM DOCK, San Francisco: Dr. Addis has emphasized that when glomerular nephritis begins it does so in an acute form which later ends in uremia and in a few cases in

heart failure. It is in the group having hypertensive heart failure and edema that this diet has been found useful and sodium harmful. When there is vomiting, nausea and finally uremic coma this diet may not be valuable, and in some cases sodium chloride actually seems to be of some use. The point that interested me particularly about this work is that it precedes, or perhaps one might say parallels, some other work that I have been interested in, namely the treatment of hypertension, benign hypertension preferably, by giving the patient an equivalent of Addison's disease. If one can combine a low sodium intake and a high potassium intake, perhaps with salt deprivation, one can produce by giving fairly frequent doses of a mercuric diuretic something equivalent to the Goldblatt hypertensive dog with its adrenals removed. In that state the dog is no longer hypertensive. I hope that the authors will extend their observations to benign hypertension and see to what extent a high potassium, low sodium intake, combined perhaps with further loss of sodium produced by mercuric diuretics, would aid in the control of that particular disorder. Of course, one reason they haven't done this is that his method of treating hypertension with thiocyanate is more effective than most methods that the rest of us have. It is natural therefore that Dr. Barker should be the last to be interested in another way of treating hypertension. In our laboratory we have seen the effect of Dr. Addis's treatment with a low salt diet, a modification of the old French or Allen methods of treating hypertension, which certainly is the most effective form of therapy. As the authors have shown, one must control the diet very rigidly. It isn't enough to tell the patient to stop taking salt. The effect of pushing that therapy to its logical conclusion, in the light of the effect of adrenalectomy on Goldblatt hypertension, should be settled within the near future. A few years ago we might have said "it isn't the hypertension that does the harm, it is the fact this patient has some toxin circulating which gives the hypertension and does the real damage." But the work with the Goldblatt dog shows conclusively that, if the hypertension can be controlled, the whole process will be greatly modified. Since the attack by surgery from the neurologic angle has not been brilliantly successful, other metabolic approaches certainly now seem very inviting.

DR. A. A. HEROLD, Shreveport, La.: The previous speaker talked of the old days of handling nephritis. Twenty years ago I was associated with a man of large experience and good ideas, and in those days the literature was full of the harmful effects of the chlorides in nephritis, and especially with edema. He said to me "It is not the chloride but the sodium radical which is doing the harm" and he suggested to me to use calcium chloride as a substitute for sodium chloride. We found a marked amelioration in the symptoms: toxicity was lower, and the edema almost invariably disappeared by substituting calcium chloride for sodium chloride in the food. That was before the days of the modern substitutes for sodium chloride which now are on the market. But by using small quantities the food was kept from being insipid. The patients got the necessary amount of chloride this way but were deprived of the sodium salt to that extent. While large quantities of the calcium chloride have a bitter taste, a smaller amount cannot be told from sodium chloride. I should like to ask the authors to state whether they have had any experience with the calcium salt and also to tell about their investigation with potassium salts.

DR. M. HERBERT BARKER, Chicago: As Dr. Addis has brought out, it is to be emphasized that this is an experimental observation, but it has definite therapeutic value in the selected case. We selected fifteen cases from a group that had been shown to be particularly sensitive to sodium chloride. No definite reason has been demonstrated for this marked sensitivity. Some individuals with a late chronic glomerular nephritis will show dramatic changes in blood pressure and urea clearance when they get salt, whether by eating anchovies, olives or Hungarian goulash; it doesn't matter where they get it. The chronic nephritic patient does not stand the resulting high blood pressure for any great period of time. We have used potassium chloride considerably, and I know

it is dangerous if given fast intravenously or if it is retained in the body. I do not have the fear of potassium that is expressed by some workers. That is probably due to the fact that we have been fortunate in not having potassium intoxication. Clinically potassium chloride has been very well tolerated in the majority of our patients during the last period of ten years during which we have been studying it. Now about the diet in Dr. Addis's rats. I should like to know what the phosphorus level was in the rats that were given meat, because in our work phosphorus was the death-dealing element when protein was administered and not the potassium. As for Dr. Dock's point about low sodium, high potassium in the hypertensive patient, it was immediately suggested when the low potassium, high sodium work came out a few years ago in the treatment of Addison's disease. We have done nothing with this phase of the minerals but it ought to be settled. As to the relation of calcium chloride, we have used it and have not found it notably helpful. We have felt that potassium chloride really entered into the system when chloride was needed and was much more satisfactory than giving the calcium salt, which is broken down in the intestine and the calcium goes out, leaving a free chloride ion which may throw some patients into an acidosis.

## TORSION OF THE TESTICLE

JOHN K. ORMOND, M.D.

DETROIT

Torsion of the spermatic cord is now a well established clinical entity, but the individual practitioner meets it so infrequently that in a large proportion of cases it goes unrecognized.

The first authentic report was by Delarsivue in 1840. In 1936 Abeshouse<sup>1</sup> was able to find 350 instances reported in the literature, which he summarized in a splendid and exhaustive article. The largest individual series were eighteen cases reported by Terazzi and nine cases by O'Connor.<sup>2</sup> To date twelve instances of this condition have come under my observation, two of which have previously been reported.

Although the condition is uncommon, its recognition is of considerable importance, for failure of recognition may result in a testicular atrophy which might have been prevented, and this assumes greater importance in view of the fact that in twenty-four of Abeshouse's 350 cases the condition was bilateral. It is undoubtedly true that in some of the instances of testicular atrophy encountered in the course of routine physical examination the disease is due to previous and usually unrecognized torsion. Atrophy of the testicle is usually due to mumps, trauma (including operation for hydrocele, hernia or varicocele) or torsion. The atrophic testicle of mumps is usually soft and extremely sensitive, while that due to trauma or torsion is firm and insensitive. The undeveloped testis is small and soft but not unduly sensitive.

Torsion has been observed in every decade of life from infancy to old age, though most commonly in adolescence or early adult life. It apparently occurs about as often on one side as on the other, but definitely oftener with maldescent of the testicle than with

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1. Abeshouse, B. S.: *Torsion of the Spermatic Cord: Report of Three Cases and Review of the Literature*, Urol. & Cutan. Rev. **40**: 699 (Oct.) 1936.

2. O'Connor, V. J.: *Torsion of the Spermatic Cord: Report of Two Cases and Review of the Literature*, Surg., Gynec. & Obst. **29**: 580 (Dec.) 1919; *Torsion of the Spermatic Cord*, *ibid.* **57**: 242 (Aug.) 1933.

complete descent. In this connection it is interesting to note that eleven cases of torsion of an intra-abdominal testis are on record.

Two types of torsion are described, intravaginal and extravaginal. Of these the intravaginal type has been observed much oftener than the extravaginal.

In intravaginal torsion the twist in the cord is within the tunica vaginalis and involves the testis and epididymis but not the tunica. Ordinarily the reflection of the parietal layer of the tunica over the epididymis forms a "mesentery" (mesorchium) running from the globus minor to about the middle of the globus major. In many recorded cases this has been much shortened, including only the globus major and hence predisposing to torsion, which may follow slight muscular strain or effort and not necessarily require unusual force.

In extravaginal torsion the twist occurs in the cord outside the tunica and the whole testicular mass is involved. This is often caused by gross violence, though a strong contraction of the cremasteric muscle is said sometimes to cause it.

The first effect of rotation is flattening of the veins and partial obstruction of the venous return; then, as the rotation continues, there occurs obliteration of the veins and finally obliteration of the artery. The effect on the testicle depends on the degree of torsion. If the venous return is not completely obstructed there will be congestion and edema, especially of the epididymis, which is more distensible than the testis. If the venous return is entirely obstructed, congestion is greater and necrosis occurs in a short time. Of course if the twist is sufficient to obliterate the artery prompt infarction occurs.

In some instances, at operation the testicle has been found to be necrotic but no torsion has been demonstrable. In view of the typical character of the attack, it is probable that in these cases torsion had occurred and detorsion had taken place after necrosis had resulted. If detorsion is brought about soon enough necrosis or atrophy may be prevented, though repeated incomplete torsion by causing repeated congestion may eventuate in atrophy.

The majority of cases reported in the literature are of complete strangulation with resultant gangrene. Since the symptoms are severe, operation has often been performed, usually orchidectomy. In some instances, however, detorsion has been possible when the condition was seen early, and there are a few instances of repeated attacks of incomplete torsion with spontaneous detorsion and a smaller number in which attacks of incomplete torsion recurred over a fairly long period and were repeatedly treated by manual detorsion. We have seen these types.

The direction of the twist is not always the same, but O'Connor stated that in the majority of acute attacks the twist has occurred from within outward.

Diagnosis presents some difficulties, especially in the first attack and when, as usually occurs, the patient is seen in one attack only.

The onset is usually sudden and has occurred during sleep, awakening the patient. More often it follows effort or slight and seemingly inadequate trauma, such as that due to diving or bicycle riding. The pain is sharp, its intensity varying with the completeness of the twist. A history of previous similar attacks, clearing up spontaneously, is of extreme importance and almost diagnostic when obtained, and the absence of any history or symptoms of gonorrhea is important.

General symptoms may include nausea, vomiting and occasionally shock. Usually there is no fever, though there may be a slight elevation of temperature. There is usually no leukocytosis.

The urine is generally clear, and urinary symptoms are usually absent. The prostate and seminal vesicles usually present no abnormalities, though there is nothing to prevent torsion from occurring in a man whose prostate is infected.

The affected testicular mass will be found drawn up toward the inguinal region and is usually exquisitely tender, often so tender, in fact, as to prevent satisfactory palpation. Determination of the position of the epididymis is of importance. Normally the epididymis lies posterior and medial to the testis, but in the case of torsion, unless the twist is through 360 degrees or any multiple of 360 degrees the epididymis will be in an abnormal position. The degree of swelling varies and may be great enough to prevent differentiation of the parts of the mass. Therefore the position of the epididymis sometimes cannot be ascertained either because of the swelling or because of the extreme tenderness of the testicular mass. On the other hand, in attacks of recurrent torsion the obstruction to circulation is not complete and the swelling may be confined to the epididymis, making recognition of its position fairly easy.

Elevation of the scrotum is said to accentuate rather than to relieve the pain, as it does in cases of epididymitis, and Prehn called this a characteristic and almost diagnostic sign.

Torsion has been mistaken for acute epididymitis, acute orchitis, strangulated hernia, suppurative inguinal adenitis, acute hematocele and ureteral calculus.

Of these conditions the most important is epididymitis, and the differential diagnosis occasionally presents some difficulty, especially in cases of epididymitis following trauma. In this connection I have reviewed the cases of so-called traumatic epididymitis which I have observed, to learn whether any of them might have been instances of torsion. In some cases the observer's notes were inadequate for a certain diagnosis at this late date, but it seems to me significant that in only one instance labeled traumatic epididymitis did atrophy of the testicle result, and that was a case of rather extensive trauma to the suprapubic region, scrotum and thigh, accompanied by marked swelling and the formation of hematoma.

In epididymitis the pain is not so sudden or so severe as in torsion; there is usually evidence of infection in the urine, prostate or seminal vesicles or a history of recent urethritis; the temperature is more apt to be elevated, and the epididymis is apt to lie in its normal relationship to the testicle and is likely to be firmer and larger than in torsion. Also in epididymitis the tenderness tends to be localized to the region of the epididymis, while in torsion the whole mass is equally tender. Again, in epididymitis there is likely to be tenderness and swelling of the vas, and elevation of the scrotum relieves rather than accentuates the discomfort. Moreover, at the age at which torsion is most common, epididymitis is uncommon.

Orchitis except as a complication of mumps and occasionally of influenza is rare; the pain is not usually severe, and the swelling, though extensive, does not involve the cord.

Torsion has occasionally been mistaken for strangulated hernia, and the differential diagnosis may be dif-



ficult, for an undescended testicle is more apt to be affected by torsion than a fully descended one and is commonly accompanied by a hernia. Of course the general symptoms of strangulated hernia are more severe than those of torsion, and they grow progressively more severe while those of torsion progressively ameliorate. Both conditions require prompt treatment, and at operation all doubt will be resolved.

Confusion with suppurative inguinal adenitis has been reported a few times. The absence of the testicle from the scrotum and the absence of any infection draining to the inguinal glands (chancroid, for example) should put one on the right track.

In one of our cases the diagnosis of acute hematocele was made first. The patient was seen late, three days after onset, at which time there were marked swelling and discoloration. A few similar instances are on record. With hematocele the pain is never so severe and there is not the retraction of the testicular mass seen with torsion.

Prompt diagnosis is important, for on it may depend the health of the affected testis. Of course if the twist has been sufficient to cause infarction, delay makes no difference; but if the patient is seen before necrosis has occurred, prompt diagnosis and prompt treatment may preserve the life of the affected testis.

The best treatment is immediate operation. The scrotum should be incised and the testicle delivered. If it is necrotic, it can then be removed; if it is not necrotic and if the twist is in the cord, the torsion can be relieved, and if it is intravaginal, the tunica can be slit and the twist reversed. In any event it is best to incise and invert the tunica and then suture the cord and testicle to the scrotal septum in such a way that torsion becomes impossible.

Sometimes spontaneous detorsion occurs, and sometimes manual detorsion is possible without incision; but in either event operation shortly thereafter is desirable to eliminate any possibility of recurrence.

In the majority of recorded cases, necrosis had occurred and either orchidectomy was done or atrophy followed.

In view of the fact that in twenty-four of 350 cases on record the condition was bilateral, and in view of the fact that congenital abnormalities such as might predispose to torsion tend to be bilateral, I advocate operation on the remaining testicle to prevent a like misfortune involving it.

#### REPORT OF CASES

CASE 1.—A youth aged 19, half an hour after doing some high diving, noticed an aching sensation in the scrotum. This was followed by marked swelling but not by discoloration. Examination three days later showed marked enlargement of the scrotal contents on the left side with extreme tenderness which made accurate examination impossible. The temperature was 99 F., and there were no general symptoms. The swelling gradually receded, and the patient returned to school. Two years later physical examination showed the left testis atrophic, firm and insensitive.

It is possible that, had this condition been recognized immediately, prompt operation would have saved the testis.

CASE 2.—A youth aged 17 for six years had recurrent attacks of pain and swelling of the left testicle. The symptoms came on suddenly, disappeared rather quickly and were not associated with fever. At the end of the last attack, as it was subsiding, the testicle swelled again and there was a temperature of 101 F. When I saw the testicle three months

later it was still larger than the right and was firm, somewhat irregular in shape and insensitive. The Wassermann test and the Aschheim-Zondek test were negative. It is my impression that the patient had recurrent attacks of incomplete torsion, eventuating in an attack of complete torsion with gangrene and probably infection.

There was every opportunity of saving this testicle by operation, either during an attack or between attacks. I have advised a prophylactic operation on the other testicle.

CASE 3.—A boy aged 13 awoke one morning with pain in the left testis without any apparent cause. A few hours later, when he was examined, there were moderate swelling and exquisite tenderness of the left testis. The seminal vesicles were not palpable, and there were no urinary symptoms. A diagnosis of torsion was made and an attempt made to untwist the testis. This was unsuccessful and apparently increased the pain. Operation was therefore performed, about twelve hours after the onset of symptoms. At operation the testis was found to be mottled but not black. There were two twists of the testis on the cord, and these were released; the testis was replaced and sutured in such a way that torsion would be impossible in the future. This testis is now shrunken to half the size of the other and is firm and insensitive. Since then I have operated on the other testis and have sutured it in such a manner that a twist would be impossible.

It might have been wiser in this case not to have attempted manipulative detorsion and to have operated immediately, though the probabilities are that the torsion was complete from the first.

CASE 4.—A man aged 22 while doing some heavy work noticed pain in the right inguinal region, and later swelling appeared. There were no fever, no history of venereal disease, no abnormality of the prostate or seminal vesicles and no urinary symptoms. The right testicle was markedly swollen and tender. At operation the epididymis was found to be anterior to the testicle; both testis and epididymis were dusky, especially the epididymis, and neither bled when punctured. The testis was removed and found to be completely infarcted.

I would now advise operation on the other testicle.

CASE 5.—A boy aged 7 years for several weeks complained repeatedly of discomfort in the right side of the scrotum, which was relieved on some occasions by lifting and rotating the testicle. In one attack the testicle became somewhat swollen, and operation was decided on. At operation the right testicular mass was found to be twice normal size. The tunica was thick and edematous, and the testis lay within it, upside down. The tunica was inverted about the cord, and the cord and testis were sutured to the septum. The boy has been completely relieved of symptoms and the testis seems normal.

CASE 6.—A strong, well developed boy of 13 noticed an ache in his lower left quadrant after a boy scout hike, and his left testicle became swollen, tense and tender. His physician advised a suspensory. Two weeks later, when seen by me, the left testicular mass was three times normal size, tense, firm and not at all tender and did not transmit light. A month later it was about normal in size but was unduly firm. The patient has not been heard from for eight years, but the testis is probably atrophic.

I would now advise operation on the other testis.

CASE 7.—A man aged 38 without any apparent reason had pain in the right groin which later involved the right testis. When he was first seen, a week later, his temperature was normal, his urine was clear, there was no urethral discharge and the prostate gave no evidence of infection. The right testicle was held high in the scrotum, and the epididymis was somewhat swollen, firm and tender and lay somewhat lateral to the testis. Ten days later the epididymis was still enlarged and a little indurated.

In the absence of any evidence of infection, I considered this a case of incomplete torsion.

CASE 8.—A man aged 34 noticed one night that without cause his left testis had swelled and become tender. The next day the swelling became less and the tenderness largely disappeared. The epididymis was found to be somewhat swollen and lay lateral to the testis. Four days later there was no abnormality.

This was undoubtedly a case of partial torsion, with spontaneous detorsion. The patient has not been seen for six years. Under similar circumstances I would now advise operation to prevent recurrence.

CASE 9.—A young man aged 19 was seized with sudden terrific pain in the left lower quadrant of his abdomen, with no apparent cause, and became nauseated and vomited. There were no urinary symptoms. He was rushed to the hospital by his friends. Examination showed slight tenderness in the left lower quadrant. The left testis was drawn up high in the scrotum and was extremely tender. The cord and testis were manipulated, with spectacular and immediate relief of symptoms. He has not returned for observation but two years later is reported to be in good health and to have had no more attacks. I have advised him to have the testis operated on to prevent recurrence.

CASE 10.—A boy aged 4 years was brought in by another physician with a diagnosis of strangulated testicle. Operation showed torsion and infarction. The testicle was removed.

In such a case I would now advise operation on the other side.

CASE 11.—A physician aged 27 complained of a sudden attack of epididymitis and gave a history of repeated sudden attacks of pain and swelling of the left testis, with recovery in a day or two. The attacks usually followed slight trauma, though in a few instances there was no exertion or trauma to explain it. There had been at least twenty-five attacks during the past twelve years, and the patient had consulted many physicians, surgeons and urologists, who had all made a diagnosis of epididymitis. He was seen by us in three attacks and was taught to undo the twist immediately after it occurred. There was always one complete twist clockwise. He has been so successful in detorsion that, although there have been several attacks since, he has never come in for the operation which was recommended.

CASE 12.—A man aged 42 complained of pain in the right side of the abdomen, which had come on suddenly two days before, during coitus. The pain had been intermittent, had not radiated and had not been accompanied by urinary symptoms or by nausea or vomiting. There was no history of previous attacks. There was some tenderness and muscular resistance on the right side of the abdomen, with its maximum in the region of McBurney's point. The right testis was absent from the scrotum. A McBurney incision was made and a mass found consisting of a black and swollen testis, with one complete twist to the pedicle. It was removed with the appendix, which showed signs of mild chronic appendicitis.

#### SUMMARY AND CONCLUSIONS

I have reviewed briefly the symptoms and results in cases of torsion of the testicle and have reported twelve new cases. I wish to emphasize the importance of prompt recognition of this condition and would stress the following elements in the diagnosis: 1. The age of the patient. In this series eight patients were under 23, the youngest being 4 years old and five being adolescents. 2. The sudden onset. 3. The severity of the pain. 4. The absence of history or evidence of genito-urinary infection. 5. The position of the affected testicle in the scrotum. 6. The position of the epididymis with reference to the testicle. 7. The tenderness of the testicle. 8. Prehn's sign.

Finally, I would emphasize my conclusions regarding treatment. I believe that in an acute attack prompt

operation offers the best chance of a healthy testicle; that even though an attack is relieved by manual or spontaneous detorsion, operation should be done soon to prevent recurrence, and that if, because of torsion, a testis has become atrophic or has been removed, operation should be done on the remaining testis to prevent a like fate befalling it.

#### ABSTRACT OF DISCUSSION

DR. ROGER W. BARNES, Los Angeles: Torsion of the testicle is probably undiagnosed more often than it is recognized. Not long ago a patient was referred to me, and both the referring pediatrician and the hospital house officer stated that he had never before heard of the condition. Dr. Ormond's report of twelve cases shows that he has been on the alert to recognize the condition. I should like briefly to report a case in which there were unusual symptoms. A boy aged 14 was awakened by a sudden severe pain in the left testicle. A physician was called, who found the testicle extremely tender and slightly swollen and the cremasteric muscle contracting and relaxing so that the movement of the scrotum was very noticeable. The next morning the pain in the testicle was still present but not severe. The patient, however, complained of frequent urination and urgency and of having noticed some blood at the end of urination. The temperature was 103 F., and further examination showed the testicle to be very tender but no larger than it had been the night before. There was considerable tenderness in the lower left part of the abdomen just above the groin. When I saw the patient that afternoon the temperature was 101.2 F., and the other manifestations were approximately the same as those observed in the morning. The testicle was tipped somewhat upward, so that the isthmus of the epididymis was below instead of posterior to the testicle. Urinalysis showed many red blood cells, an occasional pus cell and a few gram-negative rods and gram-positive cocci. A roentgenogram showed no evidence of urinary calculi. The leukocyte count was 9,200. At operation some edema of the cord was found, but no torsion was present. The testicle was somewhat congested but otherwise normal. Fixation of both testicles, as Dr. Ormond has advised, was done, and the boy made an uneventful recovery. I am not certain whether some other pathologic process produced the fever, the tenderness in the lower left part of the abdomen and the blood in the urine, or whether these manifestations were all due to the torsion of the testicle. I should like to have Dr. Ormond's opinion regarding this.

DR. JAMES A. MAY, San Diego: Dr. Ormond has given a comprehensive discussion of torsion of the testicle. The twelve cases which he has reported constitute a rather large individual series and give his paper especial value and interest. There has been considerable speculation regarding the underlying etiologic factors in torsion. A thorough knowledge of the embryologic development of the testis and the mechanism of testicular descent is necessary for a complete understanding of the abnormal anatomic characteristics. The predisposing factors, according to Hinman, are (1) an anomaly of the tunica vaginalis which may be too large or have too high an insertion on the cord or an abnormal reflection from the epididymis; (2) absence or too great length of the gubernaculum; (3) an unusually low insertion of the cord; (4) an anomaly of the attachment of the epididymis to the testicle making the mesorchium loose or too short, and (5) an anomaly of the attachment of the testis and epididymis to the scrotum, so that this attachment is too loose. A voluminous tunica vaginalis per se would not seem to be a logical etiologic factor if one may judge from the frequency with which hydrocele occurs. I believe that the abnormal reflection from the epididymis is a much more important factor, in that it allows the testicle and the epididymis to hang in an intravaginal position which invites torsion. Absence or too great length of the gubernaculum does not seem to constitute a logical offender, since intermittent testicular retention is common in boys. The abnormal or loose attachment of the epididymis to the testicle, which causes the testicle to hang in an eccentric manner, is a much



more important factor. In addition, there are external factors which concern the force that precipitates the twist. Violent trauma, such as a direct blow, may tear the testicle loose from its scrotal attachments, thus permitting torsion to occur. Torsion has followed walking, heavy lifting, sneezing or straining at stool. It has also occurred during sleep. Many writers believe that a strong contraction of the cremasteric muscle initiates the twist, but this cannot be considered a factor in the causation of abnormally retained testes. The conclusion regarding the cause of torsion is that no one factor is responsible in all cases and that several factors may play a part in any one case.

DR. JOHN K. ORMOND, Detroit: I have never seen a case like the one described by Dr. Barnes. Hematuria has not occurred in any of the cases I have observed. Dr. Barnes's emphasis on teaching is apropos. I thank Dr. May for his discussion of the cause, which adequately complements my paper.

## EXCRETION OF SULFANILAMIDE AND ACETYSULFANILAMIDE IN HUMAN MILK

SHERMAN S. PINTO, M.D.

OMAHA

With the introduction and widespread use of sulfanilamide in the treatment of puerperal infections, much work has been done on the effect of the drug on the sick mother.<sup>1</sup> The excretion of the drug in men and in nonlactating women has also been studied extensively,<sup>2</sup> but I have been unable to find any work on the excretion of sulfanilamide in the lactating human mother. This work was undertaken to study the possibility of excretion of sulfanilamide in human milk and to determine, if possible, the amount of both sulfanilamide and the conjugated form of sulfanilamide which are known to be present in human blood<sup>3</sup> and, therefore, could possibly be present in human milk.

### PROCEDURE

The method described by Marshall<sup>2</sup> in which alcohol is used as a protein precipitant cannot be applied to milk because of the high fat content of milk. An appreciable amount of fat is dissolved by the concentrated alcohol and later is precipitated during the process of diazotization. In cow's milk, the method described by Fuller,<sup>4</sup> in which trichloroacetic acid is used as a protein precipitant, works satisfactorily. Apparently there is enough protein present so that the fat of the milk is enmeshed by the protein coagulum, and fat and protein are removed at the same time. In human milk the ratio of fat to protein is much higher, and the protein precipitants that I used failed to form a coagulum which would at the same time enmesh and remove all the colloidal fat. I have overcome this difficulty by making the analyses on "skimmed" human milk. The milk is centrifuged for ten minutes at 3,500 revolutions per minute. Sulfanilamide added to human milk has been recovered quantitatively from the skimmed portion

of the milk, and none was lost by dissolving in the fat which was removed by centrifugation. Since the fat content of the milk in the "cream" layer varied from 3 to 4.5 per cent, it was found more satisfactory to report all results in terms of "skimmed" milk. Diazotization of the sulfanilamide with dimethyl-alpha-naphthylamine was used because the color produced was extremely sensitive to small variations of the sulfanilamide content of the sample undergoing examination. Certain conditions were found to produce maximum color, deviations from this optimum resulting in lessened color production. The conditions for optimal results are that (1) the solution should contain 0.01 normal hydrochloric acid, (2) the solution should contain 47 per cent alcohol and (3) the trichloroacetic acid concentration should be kept as low as possible because it retards the diazotization process. To 1 cc. of skimmed milk are added 1 cc. of 20 per cent trichloroacetic acid and 2 cc. of water. The mixture is filtered, and 2 cc. of the clear filtrate is pipetted into a 15 cc. test tube. To this are added in succession 1 cc. of tenth normal hydrochloric acid, 5 cc. of 95 per cent alcohol, 1 cc. of 0.1 per cent sodium nitrite and, after waiting three minutes, 1 cc. of the dimethyl-alpha-naphthylamine reagent. (The dimethyl-alpha-naphthylamine reagent is made by dissolving 1 cc. of dimethyl-alpha-naphthylamine in 95 per cent ethyl alcohol and diluting to 100 cc.) A suitable standard should be prepared at the same time. It is important that the standard should also contain trichloroacetic acid, for this imparts an orange tinge to the final color, thus facilitating the color comparison. Maximum color development occurs in thirty minutes and remains constant for several hours.

It has been shown that, at least for dogs, acetylsulfanilamide is more toxic than free sulfanilamide. Therefore, I have extended my studies to include determination of this substance in human milk. When a protein-free filtrate of milk, prepared by using trichloroacetic acid, is heated with normal hydrochloric acid to hydrolyze the acetylsulfanilamide compound, the solution turns brown after about ten minutes heating at boiling temperature. I found that this charring is due to some substance or substances which are removable by treatment of the filtrate with copper sulfate-calcium hydroxide, as is done for the removal of carbohydrates. To use copper sulfate-calcium hydroxide for the removal of protein and carbohydrate, as is done for the determination of lactic acid in milk, is not suitable, since some substance is left in solution which is precipitated by the alcohol at the time of diazotization of the sulfanilamide. I found that the copper sulfate-calcium hydroxide treatment did not remove any sulfanilamide added to human milk.

Ten cc. of protein-free filtrate, prepared by adding one volume of 20 per cent trichloroacetic acid to one volume of milk and filtering, is pipetted into a 25 cc. volumetric flask. To this is added 4 cc. of 20 per cent copper sulfate and 4 cc. of a 20 per cent calcium hydroxide suspension. If the calcium hydroxide suspension has not been freshly prepared, more than 4 cc. may be necessary in order to make the contents of the flask alkaline. The contents are shaken frequently for one-half hour, diluted to 25 cc. and filtered. Five cc. of the filtrate (equivalent to 1 cc. of milk) plus 1 cc. of six normal hydrochloric acid are put into a test tube 25 by 200 mm., covered with a small beaker and placed in boiling water for thirty minutes. After

Eli Lilly & Co. furnished the sulfanilamide used in this work.  
From the University of Nebraska College of Medicine, Department of Biochemistry.

Dr. Sergius Morgulis showed continued interest and gave advice throughout the course of this work.

1. Colebrook, Leonard, and Kenny, Méave: *Treatment of Human Puerperal Infections and Experimental Infections in Mice with Prontosil*, *Lancet* 1: 1279 (June 6) 1936.

2. Marshall, E. K., Jr.; Emerson, Kendall, and Cutting, W. C.: *Paracetamol in Human Blood*, *J. A. M. A.* 108: 953 (March 20) 1937.

3. Marshall, E. K., Jr.: *Excretion of Sulfanilamide in Blood and Urine*, *Lancet* 1: 194 (Jan. 23) 1937.

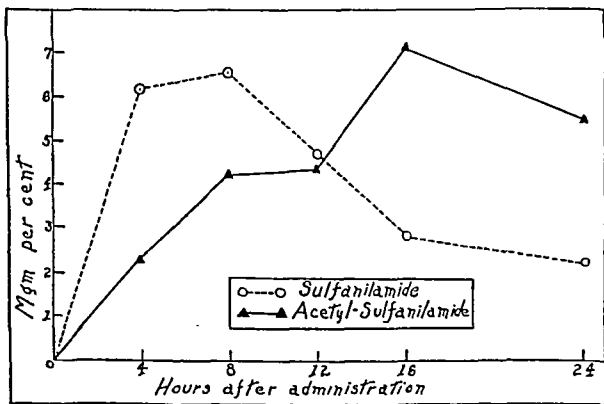
in *Prontosil Therapy*.

cooling, one drop of phenolphthalein is added and the hydrolyzed mixture is neutralized with concentrated sodium hydroxide solution. The liquid is then transferred to a 10 cc. volumetric flask and diluted to volume. Five cc. of this diluted material (equivalent to 0.5 cc. of milk) is pipetted into a 25 cc. test tube and the analysis for sulfanilamide is made as originally described by Marshall<sup>2</sup> for sulfanilamide in urine. To the 5 cc. of filtrate are added 5 cc. of water, 2 cc. of tenth normal hydrochloric acid, 5 cc. of 95 per cent ethyl alcohol, 1 cc. of 0.1 per cent sodium nitrite and 1 cc. of the dimethyl-alpha-naphthylamine reagent. It is not necessary to treat the standard with trichloroacetic acid, copper sulfate or calcium hydroxide. The trichloroacetic acid in the milk filtrate is decomposed on hydrolysis and does not affect the final color produced. The copper sulfate-calcium hydroxide treatment of the filtrate does not influence the color production.

CLINICAL RESULTS

In the lactating woman a study was made of the excretion of both sulfanilamide and the acetylated compound in the milk and urine.

The patients used in this report had been delivered of normal babies several days previously and had normal kidney function. During the period of the study the babies were placed on an artificial formula. The patients were given 4 Gm. of sulfanilamide in divided doses at 7, 8 and 9 a. m. For the next twenty-four hours no change was made in the diet or fluid intake. The urine was collected for twenty-four hours and the total amount of sulfanilamide and acetylsulfanilamide excreted in it was determined.<sup>2</sup> The milk was collected every four hours, the breasts being pumped dry, and determinations of the sulfanilamide and acetylsulfanilamide content were made for the twenty-four hour period. The entire amount of sulfanilamide administered was not excreted during that time but the amount left in the body was not sufficient to influence the results. Table shows the results obtained.



Excretion of sulfanilamide and acetylsulfanilamide in human milk.

On the chart and in the table it can be seen that the peak of excretion of conjugated sulfanilamide in milk occurs several hours later than the peak of excretion of free sulfanilamide in milk. Both these curves are similar in shape to the concentration of sulfanilamide in the blood as described by Marshall,<sup>2</sup> with the difference that in blood the peak of the concentration of the drug occurs several hours earlier than it does in the milk.

COMMENT

The concentration of sulfanilamide in human milk after the ingestion of a single large dose of the drug follows a course similar to that found by other workers for its concentration in blood.<sup>5</sup> The only difference is that the peak of concentration in milk seems to lag behind that in the blood by several hours. The concen-

Excretion of Sulfanilamide and Acetylsulfanilamide in Human Milk for the First Twenty-Four Hours After Ingestion by Mouth

Pa- tient	Hours After Drug Adminis- tration	Milk				Urine		
		Vol- ume, Cc.	Sulfanilamide Content		Acetylsulf- anilamide Content		Sulf- anil- amide, Gm.	Acetyl- sulf- anil- amide, Gm.
			Mg.	Mg. %	Mg.	Mg. %		
L. K.	4	31	1.9	6.1	0.7	2.2		
	8	75	5.0	6.6	3.2	4.3		
	12	90	4.2	4.7	4.0	4.4		
	16	112	3.3	2.9	8.5	7.6		
	24	120	2.8	2.3	6.6	5.5		
	Total	428	17.2		23.0		3,225	0.33
M. T.	4	39	1.2	3.0	2.3	5.9		
	8	32	2.0	6.1	2.0	5.2		
	12	21	0.9	4.3	1.4	6.6		
	16	36	1.2	3.2	2.9	8.1		
	24	43	1.1	2.5	2.6	6.0		
	Total	171	6.4		11.2		1,500	0.23
D. M.	4	18	0.9	5.0	0.3	1.5		
	8	70	4.1	5.9	1.3	1.9		
	12	43	1.6	3.7	1.9	4.4		
	16	22	0.6	2.9	1.0	4.5		
	24	132	2.3	1.7	5.3	4.0		
	Total	285	9.5		9.8		3,400	1.54

tration of acetylsulfanilamide in milk has a similar concentration curve except that the peak of concentration occurs several hours later than the peak for free sulfanilamide. Analysis of separate samples of milk shows no tendency on the part of the breast tissue to concentrate the drug in the milk. In fact, from the evidence at hand it would seem that the concentration of the drug in the milk is directly dependent on the level in the blood and that when the blood level falls there is a similar fall in the level of sulfanilamide in the milk. This would seem to be accomplished by reabsorption of the drug into the blood from the milk, thus tending to prevent dangerous accumulation of the drug in the milk. This mechanism prevents nursing infants from ingesting harmful amounts of the drug from the milk.

A study of the figures for L. K. in the table shows that, while the patient secreted 428 cc. of milk during the twenty-four hour test period, this milk contained a total of only 17.2 mg. of free sulfanilamide and 23 mg. of acetylsulfanilamide, calculated as sulfanilamide. More than half the dose of sulfanilamide was excreted through the kidneys in the first twenty-four hours after administration. This is certainly an example of the general principle that noxious drugs are rarely secreted in the milk of nursing mothers in quantities sufficiently large to harm the nursing infant.

Theoretically, any nursing baby under 1 year of age will not take more than 1,200 cc. of milk a day. If the mother's blood level of sulfanilamide should be kept at 10 mg. per hundred cubic centimeters for the full twenty-four hours, the baby would not receive more than 0.12 Gm. of sulfanilamide and about 0.16 Gm. of acetylsulfanilamide. This dosage of the drug would not be harmful to any baby except one very allergic to sulfanilamide.

5. Scudi, J. V.: Determination of Sulfanilamide in Biological Media, J. Biol. Chem. 122: 539 (Jan.) 1938. Marshall, Emerson and Cutting.<sup>3</sup>

## SUMMARY

A method has been devised for the determination of sulfanilamide and acetylsulfanilamide.

From the limited series reported, it would seem that the amounts of sulfanilamide or acetylsulfanilamide excreted in human milk, when therapeutic doses are given to the lactating mother, is not ordinarily harmful to the normal nursing infant.

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## ANEMIA DURING SULFANILAMIDE THERAPY

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BALTIMORE

Acute anemia associated with the administration of sulfanilamide was first described by Harvey and Janeway.<sup>1</sup> Three cases were reported, and the accounts of two additional cases were later published by Kohn<sup>2</sup> and Willis.<sup>3</sup> Except for these few reports very little emphasis has been laid on the development of severe anemia as a complication of sulfanilamide therapy.

During the past year 522 patients have received sulfanilamide<sup>4</sup> in the Johns Hopkins Hospital. By far the commonest serious toxic complication observed in this series of cases has been the development of acute anemia. A special study of the cases in which anemia developed has been undertaken and the significant data obtained are reported in this paper.

## INCIDENCE

The incidence of acute anemia associated with sulfanilamide therapy is considerably higher than one might judge from the scarcity of reports in the literature. Among the 522 patients treated with sulfanilamide acute anemia developed in twenty-one, or 4 per cent. It is of interest that the incidence among children was higher than among adults. One hundred and forty-four children received the drug and acute anemia developed in twelve (8.3 per cent), whereas there were only nine cases of acute anemia among the 378 adults treated (2.4 per cent). Agranulocytosis was much less common than acute anemia, there having been but one case in the entire series.

## PREDISPOSING FACTORS

No definite predisposing factors were noted in the analysis of cases of acute anemia, but the following should be discussed briefly:

(a) *Type of Infection.*—The twenty-one patients in whom acute anemia developed were suffering from various types of both acute and chronic infections, as listed in table 1. No one form of infection seemed to predominate.

(b) *Fever.*—It may possibly be of significance that all twenty-one patients had fever (in most cases over 102 F.) at some time during the period of sulfanilamide therapy. No cases of acute anemia occurred among a

large group of afebrile patients who were given sulfanilamide for prophylactic reasons or because of chronic bacilluria. In one patient, a 2 months old infant, during a high fever severe anemia developed after three days of treatment, but later, when she was afebrile, anemia failed to develop when a second course of the drug was given. Whether or not the presence of fever predisposed to the development of anemia in these cases remains open to question.

(c) *Dosage.*—The patients in whom acute anemia developed did not receive on the average any larger doses of the drug than the other patients treated with sulfanilamide. The largest dose given was 0.2 Gm. per kilogram of body weight in twenty-four hours, whereas as much as 0.47 Gm. per kilogram has been given in other cases with apparently no harmful effects.

(d) *Concentration of Sulfanilamide in the Blood.*—The highest concentration of sulfanilamide encountered in the blood was 10.7 mg. per hundred cubic centimeters. Blood levels as high as 40 mg. have been observed among patients in whom anemia has not developed.

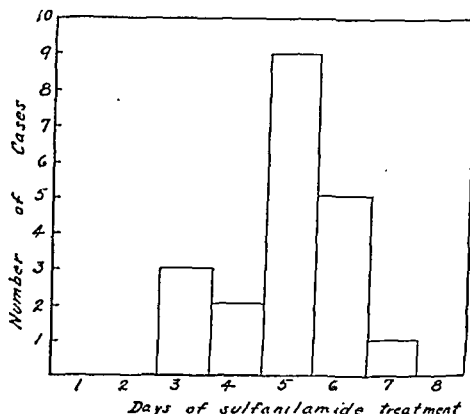


Chart 1.—Date of maximum anemia in cases of acute anemia associated with sulfanilamide therapy. Two cases were not charted because of insufficient data. Both hospital admissions of T. L. are included.

(e) *Acidosis.*<sup>5</sup>—The carbon dioxide combining power was within normal limits in all but two of the patients studied. The lowest value encountered was 33.4 volumes per cent. The carbon dioxide combining power, however, was not measured at sufficiently frequent intervals in any of the cases to rule out the possibility of a transient acidosis during the course of therapy.

## TIME RELATIONSHIP

In all cases of acute anemia in which hemoglobin measurements were made frequently, the fall in hemoglobin was shown to begin between twenty-four and seventy-two hours after the onset of treatment. The maximum anemia occurred most frequently on the fifth day, and in no case was it recorded before the third day or after the seventh day (chart 1). It should be emphasized that in the entire series of 522 cases in which sulfanilamide therapy was used no rapidly progressing anemias developed after the first week of therapy except when there was an obvious cause such as loss of blood at operation.

A second type of anemia observed occasionally during sulfanilamide therapy has been reported by Jennings and Southwell-Sander<sup>6</sup> and might be termed a "slow

From the Medical Clinic of the Johns Hopkins Hospital and University.  
1. Harvey, A. M., and Janeway, C. A.: The Development of Acute Hemolytic Anemia During the Administration of Sulfanilamide, *J. A. M. A.* **109**:12 (July 3) 1937.  
2. Kohn, S. E.: Anemia During Treatment with Sulfanilamide, *J. A. M. A.* **109**:1005 (Sept. 25) 1937.  
3. Willis, Thayer: Sulfanilamide in Ophthalmia Neonatorum, *Yale J. Biol. & Med.* **10**:275 (Jan.) 1938.  
4. The great majority of the patients were treated with sulfanilamide; a few received the closely related compound protosil (the disodium salt of 2'-azo-7'-acetyl-amino-1'-hydroxynaphthalene-3', 6' cases are reported through the courtesy of Drs. Edwards A. Park.

5. Jennings, G. H., and Southwell-Sander, G.: Anemia and Agranulocytosis During Sulfanilamide Therapy, *Lancet* **2**:898 (Oct. 16) 1937.

anemia." The fall in hemoglobin progressed slowly in their three cases, the maximum anemia occurring from two to four weeks after the start of treatment. My associates and I have observed eight similar cases of "slow anemia," but, since it is extremely difficult to determine in most instances whether the anemia is due to sulfanilamide or is secondary to a long standing infection, I have not included them in the present analysis.

#### NATURE OF ANEMIA

In their original publication, Harvey and Janeway described the acute anemia occurring during sulfanilamide treatment as a hemolytic anemia. Studies on the blood of their three patients indicated that there was rapid hemolysis associated with the fall in hemoglobin. Recently we have had the opportunity of following the entire course of a recurrent acute anemia which developed during a second course of sulfanilamide treatment. Because of the completeness of the data obtained, the case is reported in some detail:

#### REPORT OF CASE

T. L., a Negro chauffeur aged 36, first admitted to the Johns Hopkins Hospital March 15, 1937, complained of a severe sore throat. His general health had been excellent in the past. In 1922 he had had a peritonsillar abscess which required incision and drainage. Since childhood he had had frequent rather mild sore throats. Two days before admission to the hospital a cold in the head developed followed by a sore throat, which became progressively worse until he came to the hospital.

The clinical and laboratory examinations as well as the patient's course in the hospital during his first admission have been reported in detail by Harvey and Janeway (case 1) and need only be outlined briefly. The temperature was 104 F., pulse rate 110 and respiratory rate 40 per minute. The patient appeared acutely ill. No abnormalities were noted on physical examination except enlarged tonsils covered with flecks of yellowish exudate and tender lymph nodes palpable at the angles of the mandible. The blood was normal except for a leukocyte count of 19,000. Culture of material from the throat showed 95 per cent beta hemolytic streptococci.

Sulfanilamide therapy was begun on the first day and the patient received 21 Gm. of the drug over a period of five days. On the third day the throat infection appeared to be clearing and the temperature and white blood cell count had fallen to normal. The patient, however, complained of nausea and dizziness and, when two days later the temperature rose to 102.6 F., the drug was stopped promptly. On the seventh day it was noticed that the mucous membranes were pale and the scleras were jaundiced. Examination of the blood revealed a hemoglobin content of 30 per cent, a white blood cell count of 87,000 and changes in the blood smear indicative of increased activity of the bone marrow. The urine showed large amounts of urobilin but the serum bilirubin was not appreciably increased. The patient was given three transfusions during the next three days and recovery was rapid and uneventful. Just before discharge from the hospital he was given a test dose of 0.9 Gm. of sulfanilamide with no demonstrable effect on the blood.

March 6, 1938, nearly twelve months after his first admission, the patient was readmitted to the hospital with a severe sore throat of five days' duration. For two days he had had great difficulty in swallowing.

The temperature was 101.8 F., pulse rate 118 and respiratory rate 22. The patient appeared acutely ill and complained of great pain on swallowing. Again there were no abnormalities made out on physical examination except for tender enlarged cervical lymph nodes and inflamed tonsils covered with patches of white exudate. The tonsils were so swollen and edematous that they nearly met in the midline and threatened to close off the pharynx entirely. There was a slight swelling in the left peritonsillar region suggestive of an early peritonsillar abscess. Again there was a predominance of beta hemolytic streptococci in the throat culture.

As shown in chart 2,<sup>6</sup> examination of the blood revealed nothing remarkable except a white blood cell count of 18,900. The blood smear was normal. There was no immediate or twenty-four hour sickling and no increase in the fragility of the red blood cells. The icterus index was 7, examination of

TABLE 1.—Cases of Acute Sulfanilamide Anemia

Patient	Age Race Sex	Diagnosis	Days of Sulfan- ilamide Treat- ment	Total Dose of Sulfan- ilamide (Gm.)	Total Drop in Hemo- globin (per Cent)	Treatment of Anemia
T. L.	36 Negro ♂	Acute tonsil- litis (2 ad- missions)	5 4	21.9 7.8	71 58	3 transfusions 1 transfusion
I. M.	26 Negro ♀	Peritonsillar abscess	2	6.7	52	2 transfusions
L. O.	53 White ♂	Carcinoma of bladder	3	7.2	60	5 transfusions
W. B.	62 White ♂	Gonococcal urethritis	5	24.0	31	3 transfusions
G. S.	27 Negro ♀	Gonococcal salpingitis	8*	31.2	45	2 transfusions
W. C.	19 Negro ♂	Lobar pneu- monia	2	6.0	27	Iron therapy
B. L.	18 Negro ♀	Gonococcal arthritis	4	14.0	40	Iron therapy
H. C.	41 Negro ♂	Urinary tract infection	3	10.8	37	Iron therapy
V. R.	18 Negro ♂	Pneumococcal meningitis	3	13.2	50	3 transfusions
H. H.	8 Negro ♂	Acute tonsil- litis	6	31.5	62	4 transfusions
M. J.	10 mos. White ♀	Meningococcal meningitis	6	11.0	25	2 transfusions
H. B.	10 Negro ♀	Generalized peritonitis	5	25.5	63	6 transfusions
J. M.	9 mos. Negro ♀	Urinary tract infection	3	5.8	40	3 transfusions
E. B.	7 mos. Negro ♂	Pneumonia	2	1.8	26	None
S. W.	7 mos. Negro ♀	Otitis media	3	4.5	42	None
R. G.	6 White ♂	Pharyngeal abscess	4	14.4	35	2 transfusions
S. C.	2 Negro ♂	Pulmonary tuberculosis	5	7.0	31	None
M. M.	12 White ♀	Pyelo- nephritis	10†	18.0	28	2 transfusions
C. D.	10 mos. Negro ♀	Influenza bacillus septicemia	2	3.6	29	4 transfusions
R. A.	7 mos. Negro ♂	Staphylo- coccal septicemia	4	4 S	46	None
V. F.	4 Negro ♀	Scarlet fever	5	15.0	28	None

\* Second hemoglobin determination not made until eighth day.

† Maximum anemia on fifth day. Patient was given two transfusions but the drug was not discontinued until five days later.

the urine was negative for urobilin and the van den Bergh test showed no increase in serum bilirubin.

At the time of admission the question was at once raised as to the advisability of treating the patient with sulfanilamide, in view of his previous experience. At that time only one report of recurrent anemia during sulfanilamide therapy had appeared in the literature.<sup>3</sup> We had followed one patient, a 9 months old female infant, in whom anemia failed to develop

6. The laboratory studies were carried out by Dr. R. F. Howard and Mr. R. L. Sewell.

during a second course of sulfanilamide after the child had suffered a severe anemia with the first course. In addition, as already mentioned, the patient in question had been given a test dose of sulfanilamide at the end of his first hospital admission without any demonstrable effect on the blood. It was therefore quite uncertain whether on this occasion hemolytic anemia would develop if sulfanilamide were given. Because of the severity of the streptococcal infection of the tonsils it was finally decided to give sulfanilamide cautiously

globin could be detected in the urine at any time. The urine from the fourth to the eighth day was a dark amber and Dr. E. K. Marshall was able to recover a reddish pigment by ether extraction which became colorless when reduced with zinc and showed absorption bands in the same range as certain of the porphyrins. The pigment has not as yet been clearly identified.

COMMENT

From the data obtained in this case as well as in the other cases already reported, it is quite evident that the development of acute anemia during sulfanilamide therapy is associated with rapid hemolysis. The abrupt rise in serum bilirubin as shown by the van den Bergh test and icterus index, the presence of excessive amounts of bile pigments in the urine and the demonstration of free hemoglobin in the blood plasma all point conclusively to an active hemolytic process. Kohn<sup>2</sup> has reported an additional sign of rapid hemolysis, namely hemoglobinuria. However, we have been unable to demonstrate free hemoglobin in the urine of any of the twenty-one patients in the present series except in one case which was complicated by gross bleeding from a carcinoma of the bladder.

EARLY DIAGNOSIS

The early signs of acute anemia associated with administration of sulfanilamide are well illustrated by the foregoing case and may be summarized as follows:

- 1. Nausea and dizziness usually begin from twelve to twenty-four hours before the signs of anemia are detected.
- 2. Increased excretion of urobilin in the urine is often the first laboratory evidence of increased destruction of the blood.
- 3. There is an unexplained rise in temperature on the third to the fifth day of therapy.
- 4. There is a sudden drop in hemoglobin.
- 5. Hyperbilirubinemia and jaundice are present.

TABLE 2.—Cases of Acute Sulfanilamide Anemia in Which Second Course of Drug Was Given

Patient	Age	Race	Sex	Diagnosis	First Course of Sulfanilamide Therapy			Second Course of Sulfanilamide Therapy			Interval Without Treatment
					Days of Treatment	Total Dose (Gm.)	Drop in Hemoglobin (per Cent)	Days of Treatment	Total Dose (Gm.)	Drop in Hemoglobin (per Cent)	
T. L.	36	Negro	♂	Acute tonsillitis	5	21.0	71	4	7.8	58	1 year
A. D.*	4 days	Negro	♂	Ophthalmia neonatorum	14†	7.4	56	5	3.7	17	10 days
S. C.	2	Negro	♂	Pulmonary tuberculosis	7	14.0	20	5	7.0	31	5 months
S. W.	7 mos.	Negro	♀	Otitis media	3	4.5	42	6	9.0	11	9 days
J. M.	9 mos.	Negro	♀	Urinary tract infection	3	5.8	40	3	3.0	0	7 weeks

\* Reported by Willis.<sup>3</sup>  
† Second hemoglobin determination not made until eleventh day of treatment.

Chart 2.—Results of blood and urine studies in case of acute hemolytic anemia associated with sulfanilamide therapy.

and watch the blood with great care in order that the drug might be stopped immediately if signs of anemia should develop. Sulfanilamide was administered as shown in chart 2, a total of only 7.8 Gm. being given over a period of three days. The clinical response to the drug was dramatic. The temperature fell within twenty-four hours to 99.4 F. and the edema and inflammation in the throat subsided rapidly. The patient felt greatly improved on the third day, but in the afternoon he mentioned that he was slightly nauseated, and urobilin appeared in the urine. When the temperature rose to 100 F. on the following day and the hemoglobin, which was being checked every twelve hours, showed a slight drop, the sulfanilamide was stopped immediately. Fluids were forced to promote excretion of the drug through the kidneys and at the end of twenty-four hours the blood showed only a trace of sulfanilamide. In spite of the fact that the drug was stopped at the first signs of blood destruction, the anemia progressed rapidly during the next forty-eight hours, the hemoglobin finally falling to 40 per cent. The icterus index rose to 35, the van den Bergh reaction to 3.1 mg. per hundred cubic centimeters (indirect) and the patient became jaundiced and continued to excrete large quantities of urobilin in the urine. The reticulocyte count reached a maximum of 6.8 per cent on the fifth day. That the hemolytic process subsided as rapidly as it had begun is shown by the precipitous fall in serum bilirubin, which took place on the fifth and sixth days. The patient was given one transfusion of 500 cc. of citrated blood on the sixth day; thereafter he made an uneventful recovery. Blood serum drawn on the fifth day showed large amounts of free hemoglobin identified spectroscopically. No free hemo-

If every patient treated with sulfanilamide is carefully watched for the appearance of these signs, the diagnosis of acute hemolytic anemia can be made relatively early. It should be pointed out that even the earliest diagnosis may not prevent the development of a profound anemia. This is well illustrated by the case reported here, in which the anemia continued to progress rapidly in spite of the fact that the drug was stopped before the hemoglobin had dropped 10 per cent. Although the rapid fall in hemoglobin often cannot be

prevented by early diagnosis, it is only reasonable to suppose that the severity of the anemia can to some extent be controlled by early withdrawal of the drug.

#### RECURRENT ACUTE HEMOLYTIC ANEMIA

To date we know of five patients who have been given a second course of sulfanilamide in spite of the occurrence of acute anemia when they were first treated. In four of the five hemolytic anemia developed during the second course of therapy. The fifth patient escaped when treated a second time, but the absence of fever in this instance and the slightly smaller dose administered may have accounted for this exception. The data from these five cases are summarized in table 2 and serve to emphasize the danger of giving sulfanilamide to patients in whom acute hemolytic anemia has previously developed while under treatment with the drug.

#### PATHOGENESIS

Little is known about the pathogenesis of acute hemolytic anemia associated with sulfanilamide therapy. It is clear from studying the blood of patients suffering from this type of anemia that the drug acts either directly or indirectly on the red blood cells, causing hemolysis. There is no evidence that the anemia is in any way related to depression of the bone marrow, for in all the cases studied there have been signs of increased rather than of decreased hemopoiesis. However, no direct examinations of the bone marrow have been made. Thus far it has been impossible to reproduce the hemolysis by adding sulfanilamide to the blood *in vitro*. No sickle cell traits or increased fragility of the red blood cells have been detected in any of the cases. The Donath-Landsteiner test has consistently given negative results.

Acute anemia associated with sulfanilamide therapy must be classed as a drug idiosyncrasy, especially in view of the fact that the majority of patients who have once suffered an attack appear to be susceptible to recurrent attacks. The exact mechanism whereby the drug causes hemolysis must await further study of the blood of susceptible persons.

#### TREATMENT AND PROGNOSIS

The treatment of acute sulfanilamide anemia consists of two measures: (1) immediate withdrawal of the drug and (2) blood transfusion. That the first of these measures alone may not be effective, even when carried out early in the course of anemia, has already been emphasized. The response to blood transfusions has in all cases been satisfactory. No deaths from hemolytic anemia have been reported.

#### CONCLUSIONS

From the study of twenty-one cases of acute anemia associated with sulfanilamide therapy the following conclusions may be drawn relating to the management of patients under treatment:

1. The hemoglobin should be measured at daily intervals during the first week of treatment and once or twice a week thereafter as long as the treatment is continued. The urine should be examined frequently for urobilin during the first week, and all unexplained febrile reactions should be looked on with suspicion. The patient should be asked frequently about subjective symptoms such as nausea and dizziness, and jaundice should be carefully watched for.

2. At the first signs of the development of hemolytic anemia sulfanilamide should be withdrawn, fluids forced

and the patient's blood matched for transfusion. If the hemoglobin falls to dangerously low levels, repeated transfusions are indicated.

3. Patients who have once suffered from acute hemolytic anemia during sulfanilamide treatment should not again be given the drug.

#### SUMMARY

1. Twenty-one cases of acute anemia associated with the administration of sulfanilamide, in a series of 522 patients treated with the drug, were studied. The incidence was higher in children (8.3 per cent) than in adults (2.4 per cent). No definite predisposing factors were noted in an analysis of the twenty-one cases.

2. The earliest signs of the anemia appeared between twenty-four and seventy-two hours after the onset of treatment. The maximum anemia occurred usually on the fifth day, and in no case did it occur before the third or after the seventh day.

3. The anemia has been shown conclusively to be associated with acute hemolysis, but the pathogenesis is at present not known.

4. Four out of five patients in whom acute anemia had developed when first treated with sulfanilamide suffered recurrences when a second course of the drug was given.

5. The anemia is treated by the immediate withdrawal of sulfanilamide, the forcing of fluids and blood transfusions. There have been no deaths reported.

6. It is important that the hemoglobin be watched carefully during the first week of sulfanilamide therapy.

### *Clinical Notes, Suggestions and New Instruments*

#### RECOVERY FROM SUBACUTE INFECTIOUS ENDOCARDITIS FOLLOWING PRONTOSIL THERAPY

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Recovery from subacute infectious endocarditis is of such uncommon occurrence that the account of such a case seems worthy of record.

*History.*—O. H., a Negress aged 39, who entered the University of Kansas Hospitals April 13, 1938, complained of chills and sweats. The family history was negative. In 1930 the patient was admitted to this hospital with tonsillitis and arthritis. At that time a tonsillectomy was performed. She remained in the hospital from April 20 to May 4. Examination of the patient showed, in addition to the arthritis, a systolic murmur at the apex and a diastolic murmur over the aortic area and down the left sternal border. The diagnosis at that time was acute rheumatic fever, chronic tonsillitis, aortic insufficiency and mitral insufficiency.

The patient has been followed in the outpatient department for the past eight years and there are repeated notes regarding the presence of mitral and aortic murmurs. On several occasions she has shown marked cardiac failure. One month before admission to the hospital the patient had an abortion, which was followed by chilly sensations and some fever. This persisted only two days, following which she felt perfectly well. One week before the present admission the patient began feeling ill and complained of chills and sweats every afternoon; she had been "up and down in bed" most of the past week.

*Examination.*—At the time of admission the patient was lying listlessly in bed with a temperature of 100.8 F. Examination of the eyes showed several small petechial hemorrhages in the conjunctiva of the left eye and also a few petechiae on the left

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check and on the left side of the neck. The fingertips were painful, and one splinter hemorrhage under the nail was seen on the right index finger. The heart was enlarged; there was a loud rough systolic murmur at the apex and a soft blowing diastolic murmur over the aortic area. The liver extended two fingerbreadths below the left costal margin. The spleen was palpable and definitely enlarged.

The laboratory examination showed red blood cells 3,940,000, white blood cells 17,300, hemoglobin 62 per cent. The urinalysis showed a specific gravity of 1.025, a trace of albumin and from 6 to 8 pus cells per high power field. A blood culture taken April 13 was positive for *Streptococcus viridans*. Blood cultures taken April 14 and 15 were likewise positive. The organism grew very readily and was typical in every respect. The sedimentation index of the blood April 13 was 30 with a vertical curve.

The patient on admission was started on prontosil<sup>1</sup> 10 cc. intramuscularly twice a day, and 10 grains (0.65 Gm.) of sulfanilamide four times a day. This therapy was continued until April 23, on which day the prontosil was given intravenously three times. The sulfanilamide by mouth was omitted because of the extreme nausea which had developed. The patient received transfusions of 500 cc. of citrated blood on April 19, 26 and 28. The patient received 10 cc. of prontosil three times a day from April 23 until April 25 and twice a day from April 26 until May 13, at which time treatment with prontosil was discontinued.

The patient's temperature, which had varied between normal and 103 F., did not go above normal on April 26 and from that time on remained normal. Blood cultures taken on April 23 and 27 and May 2, 7, 11, 17 and 20 were negative. The spleen was not palpable May 5. The blood count May 7 revealed red blood cells 4,160,000, white blood cells 7,200, hemoglobin 74 per cent. This was a marked change, particularly in the white blood cell count, which on April 22 was 23,000. The blood sedimentation curves were as follows: April 26: index 32, vertical curve; May 3: index 17, diagonal curve; May 14: index 7, horizontal curve.

Although the patient continued to be fever free, signs of cardiac failure became more and more evident. The patient's dyspnea increased, and marked edema and anasarca appeared. The patient died May 25, twenty-nine days after the temperature had become normal and twelve days after treatment with prontosil had been discontinued. Autopsy was performed two hours after death by Dr. Rae Richeson of the department of pathology.

**Autopsy.**—The anatomic diagnosis was chronic and subacute vegetative bacterial valvulitis of the mitral and aortic valves (healing bacterial endocarditis), acute and chronic myocarditis, hypertrophy and dilatation of the heart. The heart weighed 400 Gm. The mitral valve showed marked thickening and scarring, and at the apex of one of the valve cusps was a vegetation which appeared to be healing and was covered with a thin layer of scar tissue. The aortic valves were also thickened and wrinkled, and on their edges were several vegetations which appeared old and organizing. Both valves were incompetent. Microscopic sections of the mitral and aortic valves showed evidence of extensive healing. On the aortic valve deep beneath the healed surface were some clumps of gram-positive diplococci. Cultures taken from small excised portions of the mitral and aortic valves were sterile.

#### COMMENT

Recovery from subacute infectious endocarditis is admittedly very rare. Since the remarkable results reported in certain streptococcal infections with prontosil and sulfanilamide, it is obvious that this drug should be tried in the treatment of subacute endocarditis. Hussey<sup>2</sup> reports one probable case of endocarditis in which recovery occurred after the use of sulfanilamide. The diagnosis in this case would, however, seem to be open to doubt. In our case there is no question as to the diagnosis. The patient had a history of rheumatic fever and old mitral and aortic valve lesions, petechiae, splinter hemorrhages, tender

fingers, fever, enlargement of the spleen and three blood cultures positive for *Streptococcus viridans*. Necropsy showed the evidence of a recent endocarditis in the stage of healing and repair.

The question open to doubt is whether the cure was produced by prontosil or whether it was a spontaneous recovery. A review of the literature to March 1, 1938, comprising 309 articles, discloses no claims of a case of endocarditis cured with sulfanilamide. In 1925 the senior author<sup>3</sup> reported a case of subacute infectious endocarditis due to *Streptococcus viridans* but showing no embolic phenomena in which recovery occurred following the administration of intravenous gentian violet. Subsequent failures to influence this disease by the administration of gentian violet have led us to the conclusion that this was a case of spontaneous recovery, such as those reported by Oille, Graham and Detweiler,<sup>4</sup> which also showed no embolic phenomena.

There are, however, certain features of this case which suggest that prontosil acted as a curative agent. The fall in temperature, the disappearance of positive blood cultures, the change in the sedimentation curve, the disappearance of the enlarged spleen and the cessation of embolic phenomena, all following so closely the intravenous administration of prontosil, are highly suggestive. It is noteworthy that no change in the temperature occurred until prontosil was administered intravenously; also that the endocarditis was probably only of one month's duration and possibly only of one week's duration when therapy was instituted.

#### THROMBOPENIC PURPURA DUE TO FOOD ALLERGY

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In January 1937 Squire and Madison<sup>1</sup> reported three cases of thrombopenic purpura that were found to be due to sensitization to food. These cases all conformed to the usual hematologic criteria for the diagnosis of the condition. All of the patients were relieved of their symptoms following the removal of the foods found to be the causative agents, and the symptoms returned on readdition of these foods to the diet. In view of the fact that many cases have been reported which showed thrombopenic purpura due to sensitization to drugs, and in view of the relationship shown by Squire and Madison between sensitization to certain foods and the thrombocyte level in the blood, it is evident that this etiologic possibility should be considered when these cases are encountered.

It is my purpose in this short communication to record another case in which food allergy was the etiologic factor in thrombopenic purpura.

#### REPORT OF CASE

**History.**—A. L. D., a white woman aged 59, was referred by Dr. Gottlieb Werley for blood study with the clinical diagnosis of purpura, probably due to an allergy to citrus fruits. The patient presented numerous ecchymotic spots distributed over the entire body. There were also innumerable petechial hemorrhages distributed over the forearms, thighs and legs. Ecchymoses had begun to appear about six years previously as occasional areas appearing on the limbs. There were free periods when there were no lesions. The bruises had increased in frequency and number until they were almost constantly present. It required about ten days for an area to clear after the hemorrhage appeared.

Ten days previous to the first visit there appeared numerous petechial hemorrhages over the limbs. This had never occurred before. For several days the number of petechiae increased. The petechiae followed the ingestion of a large quantity of citrus fruits while the patient was visiting in a citrus fruit raising community. The patient stated that she was not particularly fond of citrus fruits although she partook of one or the other of them frequently in small quantities. There were

3. Major, R. H.: Recovery from Subacute Infective Endocarditis Following Gentian Violet Therapy, *J. A. M. A.* 84: 278-279 (Jan. 24) 1925.

4. Oille, J. A.; Graham, Duncan, and Detweiler, H. K.: *Streptococcus Bacteremia in Endocarditis*, *J. A. M. A.* 65: 1159-1163 (Oct. 2) 1915; A Further Report on a Series of Recovered Cases of Subacute Bacterial Endocarditis, *Tr. A. Am. Physicians* 39: 227-230 (May 6) 1924.

1. Squire, T. L., and Madison, F. W.: Thrombocytopenic Purpura Due to Food Allergy, *J. Allergy* 8: 143 (Jan.) 1937.

1. Prontosil is the disodium salt of 4-sulfamido-phenyl-2'-azo-7'-acetyl-amino-1'-hydroxynaphthalene-3', 6' disulfonic acid.

2. Hussey, H. H.: Probable Bacterial Endocarditis Apparently Cured with Sulfanilamide, *M. Ann., District of Columbia* 6: 273-276 (Sept.) 1937.



no subjective complaints, and the usual daily routine was being carried out as usual. Five days after the appearance of the petechiae a severe epistaxis occurred, which subsided to a slow capillary bleeding from the nasal membrane.

The essential points in the past history were as follows:

Head: Nasal congestion for many years.

Cardiorespiratory system: Normal.

Gastrointestinal tract: A marked anorexia and a distressing sense of fullness after even very small meals.

Genito-urinary tract: A severe hemorrhage after an operation on the kidney twenty-seven years previously. The details of this operation were not known. One year before admission there had been an attack of pain and hemorrhage from one kidney attributed to a stone, although no stone was demonstrable by complete x-ray and cystoscopic examination.

The menses had begun at 18 years and the menopause occurred at 52. Otherwise the menses were normal.

Other past illnesses were typhoid thirty years before and severe hives in childhood. There had also occurred the usual diseases of childhood.

The family history was insignificant except that the mother and one sister had had severe headaches for many years.

Other items in the past history were negative.

*Examination.*—The physical examination was negative except for the cutaneous lesions described. The abdominal wall was rather obese and satisfactory palpation of the spleen could not be accomplished.

Examination of the blood showed total white blood cells 5,600, total red blood cells 3,900,000, hemoglobin 12.5 Gm. per hundred cubic centimeters, neutrophil polymorphonuclear leukocytes 63 per cent, immature neutrophils 3 per cent, lymphocytes 28 per cent, eosinophils 5 per cent and basophils 4 per cent. There was slight irregularity in the size and shape of the red blood cells. In the stained smears only an infrequent platelet was seen. Direct enumeration of the platelets showed 60,000. There was no retraction of the clot after several days' standing.

The urine contained a trace of albumin, many pus cells and a few red blood cells.

Cutaneous reactions to food were negative. Intracutaneous reactions were definitely positive to orange, lemon, shrimp, avocado, apple, milk, rye, cheese and cottonseed. A number of other borderline reactions were obtained.

Leukopenic indexes were as follows: milk negative, wheat negative, egg borderline and orange positive.

A diagnosis was made of thrombopenic purpura, probably due to allergy to citrus fruits.

*Progress.*—The course of the condition confirmed the diagnosis. A diet was prescribed in which the foods giving positive reactions were omitted. No new ecchymotic areas appeared, although previously there were several new ones each day. Ten days after the diet was started the skin was practically clear. On this day the leukopenic index was done for orange juice. As already noted, the result was positive. The next day there were two large ecchymotic areas on the forearm. Before this test was done the platelet count had risen to 240,000 and the clot retraction time was normal. On the day after the test the platelet count was 100,000. After another month there had appeared no new lesions. Small amounts of citrus fruits were then added to the diet. After three days several small ecchymotic areas appeared on the limbs. The fruits were again removed from the diet and after four months there has been no return of the symptoms.

It is interesting to note that the anorexia and the sense of fullness after meals have disappeared. The platelet count is now 385,000. The remainder of the blood count is normal. The patient feels in better general health than she has for several years past.

#### COMMENT

Two thoughts seem to be indicated by this and other similar cases. First, the obvious one, that at least an unknown percentage of persons suffering from this disease might be relieved by a much simpler procedure than radical splenectomy. Certainly the results with this case were much more striking than those obtained by the more tedious and disappointing general therapy employed in the past.

Second, it is amazing that a shock organ could be so narrowly limited that only the cells responsible for the platelet formation in the bone marrow could be affected by an allergen or, on the other hand, that an allergic reaction should result in an abnormal function of the spleen (destruction of red blood cells).

#### SUMMARY

A case of thrombopenic purpura has been successfully and easily controlled by the removal from the diet of foods to which the patient was allergic.

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## Special Clinical Article

### CANCER OF THE CERVIX UTERI: RECOGNITION OF EARLY MANIFESTATIONS

CLINICAL LECTURE AT SAN FRANCISCO  
SESSION

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It is one thing to recognize cancer early, i. e. when it is first seen, but it is quite another to recognize early cancer, i. e. cancer in its incipience. It is to the recognition of early cancer that I shall confine my remarks.

When one considers that genital carcinoma comprises about 2 per cent of cancers in the male while it forms about 27 per cent of cancers in the female, its comparative importance is at once manifest. In general it may be said that of all women suffering from cancer about one third are afflicted with uterine cancer. Of these about 80 per cent have cancer originating in the cervix uteri.

The foregoing remarks would represent only statistical repetitions did they not develop the startling revelation that one of the organs most commonly involved in cancer in women is situated suitably for direct visualization, palpation and instrumentation as is no other human organ which has an equally high incidence of cancer. The obvious conclusion follows that the unequivocal diagnosis of established cancer of the vaginal portion of the cervix uteri generally is a simple matter and should follow closely on the first examination.

Equally important is it that so many patients who possess a so-called suspicious-appearing cervix, whatever that may be, should not be terrified by the fear of cancer and subjected to a long series of office treatments for the time-tattered, hysterical and questionable excuse of cancer prophylaxis, when it is possible to establish practically beyond peradventure the presence or absence of anything suggestive of cancer.

#### EARLY VISIBLE CANCER

This brings up at once the problem of recognizing the early manifestations of cervical cancers. Fortunately the majority of such cancers occur on the portion in the region about the external os. The primary prerequisites for their recognition are threefold: adequate exposure of the cervix, adequate illumination and deliberate, thoughtful inspection. There is little doubt that, if all physicians would observe these elementary

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requirements, most cervical cancers would be suspected on the first examination, while they were still comparatively early yet advanced far enough to produce slight tumefaction, a small ulcer or some other superficial change outside the normal variation, although symptoms might be entirely lacking. One would then have the desirable combination of early recognition of comparatively early cancer.

In speaking of early cancer of the cervix it may be helpful merely for the purpose of clarifying the discussion to segregate early cancer arbitrarily into two classes: cancer in that phase in which, while still small, it is clinically recognizable, and cancer in an earlier phase, in which one is not ordinarily prepared to recognize it and the gross physical aspect of the tumor is not so apparent. For descriptive purposes the latter may be considered as hidden, covert or latent cancer.

Clinically recognizable early cancer of the vaginal portion of the cervix, as physicians have been taught to recognize it, usually presents itself as a red, firm, irregular, somewhat elevated circumscribed process, situated ordinarily in the neighborhood of the external os. It generally bleeds readily on light manipulation

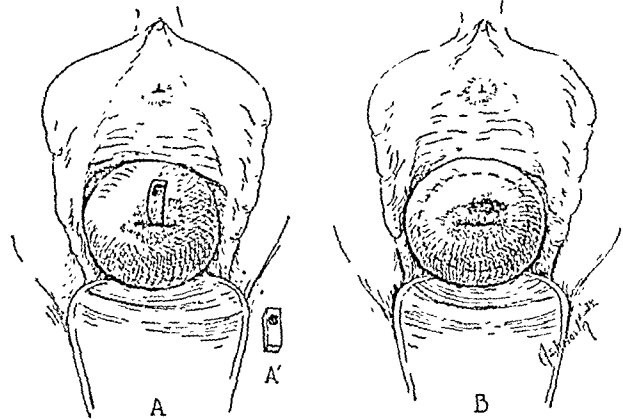
adjoining normal-appearing tissue. The block so obtained should be rectangular or nearly so, as shown in the accompanying illustration, and should immediately be fixed in solution of formaldehyde or other suitable fixing solution. If the material is obtained and prepared in this way, when it is ready for microsectioning there is little doubt about the direction in which the block should be cut. Minute fragments of tissue, wedge-shaped pieces of tissue and material obtained by scooping out tissue with the endothermy loop may be entirely unsatisfactory. The advisability of curetting the surface of the process as has been recommended is also a dubious procedure. Ordinarily there can be little excuse for such haphazard methods, when the lesion is small, circumscribed and primarily a diagnostic problem.

When the area under suspicion is more diffuse or located on a cervix that otherwise merits some form of operative correction, an amputation or a Sturmdorf procedure combined with amputation, as described by Te Linde,<sup>1</sup> is a convenient method of simultaneously obtaining material for biopsy and correcting a local pathologic condition. Whether the scalpel or the endothermy current is employed for this purpose probably matters little. However, if the latter is used one should allow for destruction by heat along the margins, where the fragment of tissue becomes unsuitable for histologic study. When a tumor is large and its character obvious, naturally observance of such minutiae is not essential.

One must of course recognize that early visible cancer probably has no distinctive gross appearance which permits its exact clinical diagnosis. Heretical as it may sound, it is also probably true that more advanced cancer possesses no distinctive or grossly pathognostic appearance. Its clinical recognition rests on the fortuitous circumstance that most ulcerating, indurated tumors of the portio are cancer.

Aside from such relatively rare lesions as those of syphilis, tuberculosis and venereal granuloma, all of which may grossly simulate cancer, the lesion which according to my experience is most commonly suspected of being an early cancer is the vermilion zone so commonly observed about the external os. This, generally referred to as an "erosion" or "ulceration," has a well marked tendency to bleed when complicated by vaginal inflammation, which renders the red surface especially susceptible to slight trauma, with the production of minute bleeding points (erosions). Generally, however, the circumstrial vermilion zone does not bleed and does not partake of the nature of erosion or ulcer.

The differentiation of a circumstrial vermilion zone of altered epithelization from an established cancer of similar size should ordinarily not be difficult. The former may be relatively smooth and flat or it may possess a fine irregularity giving it a finely granular appearance. It does not, however, appreciably change the gross contour of the cervix. If it involves both lips of the cervix, as it often does, it has its greatest expanse on the anterior and posterior lips, with narrow lateral connecting zones of red. On palpation with a sound the surfaces are found to be elastic, and under magnification cervical glands are visible pouring forth their watery secretion onto an intact, red and glistening mucosa.



Schematic representation of the method of obtaining material for histologic study. A represents a suspicious area on the anterior lip of the cervix uteri, with the dark lines indicating the direction of incisions for removal; A', the shape of the excised block of tissue, and B, a larger suspicious area, which in some cases may advantageously be removed by a cone-shaped enucleation of the endocervix, together with a portion of the portio, as indicated by the circularly dotted line.

with a soft cotton pledget and on palpation may feel indurated, although induration as a highly diagnostic sign has probably been greatly overemphasized. It is a lesion that should at once arouse one's suspicion as to its malignant character, and to discover it no apparatus is necessary that cannot be found in the office of any qualified physician. The obtaining of tissue for histologic examination without undue delay is imperative, so that one's diagnosis may be unequivocally established and treatment advised.

The obtaining of biopsy material from such a suspicious area on the vaginal portion of the cervix is in itself so important a matter that it cannot be overstressed. It may sound trite to say that material for biopsy must contain cancer before cancer can be revealed under the microscope. Most pathologists can testify to personal experience with tissue submitted to them from cancer-afflicted patients which either showed no cancer or was of debatable character while full-blown carcinoma existed a few millimeters from the site of the specimen. Tissue removed from a small circumscribed area suggestive of cancer should include both material from the suspicious area and a generous amount of

1. Te Linde, R. W.: Amputation of the Cervix with Application of the Sturmdorf Flap Principle, *Surg., Gynec. & Obst.* 43:513 (Oct.) 1926.

A small carcinoma on the surface of the portio does not have as perfect a circumstantial distribution as the common vermilion zone does, and ordinarily it is elevated, so that it alters the contour of the cervix. Its color generally offers a distinct contrast to the surrounding mucosa, while its surface is generally irregular and may show the opening of cervical glands. Palpation of the tumor with a sound reveals the irregularity previously noted and a lack of elasticity, and if there is beginning degeneration of the tumor the sound can be pushed with little force into the substance of the tumor, which then bleeds readily.

A small cancer with ulceration can so simulate a benign, nonspecific, inflammatory process of the cervix, while a benign process when complicated by induration and bleeding can so mimic cancer, that their gross differentiation may be impossible. However, such instances have so far been relatively uncommon.

Summarily, then, early cancer of the vaginal portion of the cervix that is clinically recognizable, as ordinarily encountered, presents a gross appearance which shows sufficient deviation from the normal to arouse suspicion. Obviously its true nature may not be recognized. Nevertheless, thoughtful appraisal of the lesion on the first examination should arouse sufficient concern to stimulate the proper removal of tissue for histologic study.

#### COVERT CANCER

I come now to a consideration of those processes on the vaginal portion of the cervix which, though their appearance does not correspond to the customary gross appearance of cancer, may represent an early phase of malignant change, i. e. covert cancer. Until comparatively recently such processes have been detected accidentally, on laboratory examination and have been unrecognized clinically as either potential or bona fide early nonulcerating cancer.

The ability to recognize clinically such processes represents a sort of cancer utopia which has probably been the dream of every physician at some stage of his medical career and is still the goal of many students of cancer.

The question is Have physicians reached this goal? The attempt has been made to bridge the hiatus between the phase of early tumefaction and ulceration of cancer and the antecedent covert stage, in which these changes have not occurred.

Presumably cancer of the portio vaginalis cervicis in its incipience passes through a stage in which the cells of the stratified epithelium in a localized area possess all the histologic earmarks of cancer but lack the property of invasion. I prefer to term this carcinomatoid process, limited to the normal boundaries of the epithelial zone before it has proved its destructive ability, probable beginning cervical cancer, because the expression carries a connotation of doubt. Such processes are also designated superficial cancer, cancer in situ, Bowen's disease, and carcinoid change. The term "precancerous" if ever permissible might conceivably also be used. The word, however, has such a definitive connotation that, with our present limited knowledge of cancer, it is doubtful that it can justifiably be employed.

Laying aside all theoretic considerations, one cannot say positively whether the ultimate fate of such suspicious lesions will be one of steady progression to invasion and full-blown malignancy or whether there may occur a process of regression and restitution to normal.

Similar epithelial changes are occasionally found at the periphery of bona fide cancers, and it is therefore necessary when the histologic picture of probable beginning cancer is seen to make certain that the material has not come from the margin of a full-blown malignant process.

Attention has been focused on these controversial areas of probable beginning cancer by the efforts of Hinselmann<sup>2</sup> and of Schiller.<sup>3</sup>

In the opinion of some authorities it is now possible to recognize clinically such early manifestations of presumptive cancer before the process of ulceration and prior, consequently, to the production of abnormal vaginal discharge, which is dependent on this change. The clinical methods designed to bring to one's attention areas of early covert cancer are limited in their application to the vaginal portion of the cervix uteri. The iodine test was proposed by Schiller, while Hinselmann advocated observation of the cervix under magnification with a suitably mounted binocular dissecting prism, which he has termed a colposcope.

The rationale underlying the iodine test of the epithelium of the vaginal portion of the cervix as proposed by Schiller is based on the observation of Warburg that cancer cells possess a higher sugar metabolism (glycolysis) than normal epithelium and the observation by Lahm, Schiller and others that cancerous epithelium usually shows an absence of glycogen. Since it has been shown by Langhans that iodine reacts with glycogen in living tissue the iodine test has been applied clinically to reveal areas possessing or lacking glycogen. The test, which has been given rather general use, is done simply by applying iodine in the form of Gram's<sup>4</sup> iodine solution to the cervix, which has been cleansed of its secretion. Normal mucosa assumes a mahogany brown color of varying intensity after from five to ten seconds of constant application. The iodine solution should be comparatively fresh.

#### THE COLPOSCOPE

The colposcope was devised by Hinselmann as a result of his observation of two large areas of leukoplakia (white plaques) on the vaginal portion of the cervix. Histologically these areas showed the cellular changes ascribed to cancer (mitoses, irregularity in size, shape, relationship and staining reaction of the cells) but they were limited to the anatomic confines of the epithelial zone, i. e. invasion was lacking. On the basis of this observation and a few earlier observations by von Franqué and others, which I<sup>5</sup> have discussed elsewhere, it appeared reasonable to infer that leukoplakia offered a starting point for cancer. Indeed, it has long been held by von Franqué<sup>6</sup> that cancer of the portio probably manifests itself first as a leukoplakic change and conversely that certain leukoplakic plaques are

2. Hinselmann, H.: Zur Kenntnis der präcancerösen Veränderung des Portio, Zentralbl. f. Gynäk. 51: 901-903 (April 9) 1927.

3. Schiller, W.: Untersuchungen zur Entstehung der Geschwülste: Collumcarcinom des Uterus, Virchows Arch. f. path. Anat. 263: 279-367, 1927; Zur klinischen Frühdiagnose des Portiokarzinoms, Zentralbl. f. Gynäk. 52: 1886-1892 (July 28) 1928.

4. Confusion exists regarding the type of iodine solution advised by Schiller. Since he referred to Lugol's solution in his original communication, it has been inferred by some workers that Lugol's solution as defined in the U. S. Pharmacopeia (compound solution of iodine U. S. P.) was meant. Schiller's reference, however, was to Lugol's solution as used for bacterial stain, which is the equivalent of our Gram's iodine solution (iodine 1 part, potassium iodide 2 parts, water 300).

5. Martzloff, K. H.: Leukoplakia of the Cervix Uteri: A Manifestation of Early Malignant Change? Am. J. Obst. & Gynec. 24: 57 (July) 1932.

6. von Franqué, O.: Leukoplakie und präcanceröse Veränderung des Plattenepithels, Zentralbl. f. Gynäk. 51: 898 (April 9) 1927.

destined eventually to become cancers. It therefore appeared logical to attempt to recognize these changes in their incipience, when they might be so small as to escape observation by the unaided eye. The magnification of from 10 to 15 diameters which the colposcope provides is designed to make such recognition possible and also to permit study of lesions other than leukoplakia.

Study of the cervix under magnification is interesting and informative if one controls one's observations with histologic studies. One learns that the cervix generally has a slight but definite pulsation synchronous with the heart beat; that cervical glands may open onto the portio 1 or 2 cm. from the external os through a normal stratified epithelium, which is bathed by their intermittent, crystal-clear secretion, and that glandular openings commonly occur also in the circumstrial vermilion zone and may have there small yellowish gray plugs simulating leukoplakia. Also it is not uncommon to note at the transition zone, where the pale pink of the normal stratified epithelium meets the bright red of the thin epithelium of the vermilion zone, areas where the epithelium is pale gray, almost white. Minute bleeding points (erosions) and small ulcers can be readily identified, as can also other more major deviations from the normal.

#### RESULTS OF TESTS

The question naturally arises as to how valuable these two methods are for the recognition of incipient cancer when compared with ordinary methods of careful inspection.

My experience with these methods now extends over approximately seven and one-half years. Unquestionably the iodine test is not specific for cancer or for areas of so-called probable beginning cancer. Schiller originally pointed out some of the pitfalls in this test but felt that nonstaining areas are often though not always cancerous. According to my experience the overwhelming majority of unstained areas, including areas of leukoplakia, show no histologic evidence suggestive of probable beginning cancer. Small epithelial gland plugs, vermilion areas, a proportion of superficially situated nabothian follicle cysts, areas of epithelial loss, either when superficial or, if complete, apparently when fibrin covers the base of the ulcer, epithelium involved in an underlying inflammatory process and particles of adherent inspissated secretion, together with other unexplained areas, fail to stain with the iodine. It follows that if areas that do not stain with iodine are not interpreted with due reserve they lead to endless confusion and alarm for the physician and unnecessary biopsy, cervical tinkering and hysteria for the patient.

Up to the present time I have not discovered a histologically proved area of probable beginning cancer with the iodine test, nor has the test proved to be of any more assistance than careful inspection with the unaided eye.

The altered epithelium that does not stain with iodine which occurs at the periphery of some established carcinomas has, as in Henriksen's case,<sup>7</sup> occasionally led to the suspicion and recognition of a cancer. So far, however, in most of such published instances<sup>8</sup> there

was a history of bleeding and an ulcerating cancer was present which should have been suspected from the beginning. It is, I believe, permissible to conclude that in its general application a test as unspecific as the negative iodine reaction is likely to be more confusing than it is to be helpful. Certainly, as I have noted elsewhere,<sup>9</sup> the test is not pathognomonic of a malignant condition, though it may possibly be a signal which calls for further study.

The colposcope, since it facilitates visual observation of the cervix uteri, would naturally appear to answer an unfulfilled need and to fall into the category of nasal and aural speculums, the proctoscope and the cystoscope. However, the corollary is not as apt as it sounds, for from the standpoint of the profession at large it has several drawbacks which probably will prevent its general adoption. These include the expense of the instrument, the time necessary to make a careful study and the need of extended experience to interpret correctly what one sees. The need of extended experience makes it necessary for the clinician to use the instrument regularly and to correlate the colposcopic appearance of the cervix with the histologic picture of the area in question. This requires frequent biopsies and study of the tissue by the clinician himself. The obtaining of tissue for biopsy takes the method out of the realm of simple office procedure, for if an area is sufficiently abnormal in appearance to warrant removal of tissue, removal should be carried out as described earlier in my discussion. An inadequate specimen for biopsy is probably worse than none, for it frequently makes it impossible for the pathologist to arrive at a correct interpretation. If cancer is present and the specimen does not contain any of it the patient's welfare is unjustifiably jeopardized.

However, I believe that the colposcope is a fundamental contribution to methods of visual examination of the vaginal portion of the cervix uteri. While I use it as a routine, it has been of essential value in only a few instances. So far I have discovered with it neither areas of unmistakable probable beginning cancer nor any small cancerous ulcers (established cancer) which I could not detect with the unaided eye on careful methodical examination. It is important to appreciate fully that the gross appearance of the small lesion of early established cancer, as pointed out by Hinselmann,<sup>10</sup> is not sufficiently characteristic to permit its differentiation from other nonmalignant lesions solely on the basis of its appearance through the colposcope.

#### EXPERIENCE OF VARIOUS WRITERS

A review of the more recent literature reveals a decided division of opinion, the details of which cannot be discussed here. Of fundamental importance, however, are the following observations: 1. Claims that leukoplakia of the cervix uteri is a precursor of cancer<sup>10</sup> lack confirmation at this time.<sup>11</sup> 2. Many of the histologic diagnoses of cancer made by Hinselmann have not been confirmed by disinterested pathologists to whom sections were submitted,<sup>12</sup> and there is no proof

9. Martzloff, K. H.: Recognition of Early Cancer of the Cervix Uteri, *Internat. Clin.* 4: 179 (Dec.) 1934; Early Cancer of the Cervix Uteri: The Practicability of Its Recognition Before the Stage of Ulceration, *Northwest Med.* 34: 295 (Aug.) 1935.

10. Hinselmann, H.: Die klinische und mikroskopische Frühdiagnose, *Arch. f. Gynäk.* 156: 239, 1933.

11. Schiller, Walter: Leukoplakia, Leucokeratosis and Carcinoma of the Cervix, *Am. J. Obst. & Gynec.* 35: 17 (Jan.) 1933. Borst, in discussion on Hinselmann.<sup>10</sup>

12. Winter, G.: Das Kolposkop bei der Krebsbekämpfung, *Zentralbl. f. Gynäk.* 61: 2147 (Sept. 11) 1937.

7. Henriksen, Erle: Precancerous and Carcinoid Lesions of the Cervix Uteri; with Comments on the Schiller Test, *Surg. Gynec. & Obst.* 60: 635 (March) 1935.

8. Graves, W. P.: The Detection of the Clinically Latent Cancer of the Cervix, *Surg., Gynec. & Obst.* 56: 317 (Feb.) 1933.

at this time, as has been claimed,<sup>13</sup> that 20 per cent of areas of leukoplakia that are studied are carcinomatous. 3. Some of the cases reported to show the value of the colposcope for revealing an otherwise unrecognizable early cancer are reasonably debatable from the standpoint of their acceptability. If, for example, cancer is present it may be impossible to ascertain from the case report which part of the gross lesion showed cancer,<sup>14</sup> and, in fact, the proof of cancer may not be clear.<sup>15</sup> In the case reported by Leip and Otto,<sup>16</sup> in which leukoplakia presumably of twelve years' standing under constant observation underwent bona fide cancerous change, the patient in question was not seen by the authors until a few months prior to the time of her operation, and two years prior to this her cervix had been considered suggestive of cancer and biopsy had been advised on the basis of a speculum examination without a colposcope. 4. The infrequency with which cancer is found on routine prophylactic examination is evident from the experience of Hinselmann and Köhler.<sup>17</sup> These authors examined 1,133 women in three and one third years in the municipal woman's clinic of Altona. These women represented a special group who were without other complaint and either sought examination for cancer prophylaxis (sixty-eight instances) or had been referred by other physicians for this particular type of examination because of a "suspicious" cervix. Sixteen women (1.4 per cent) of this entire highly selective group showed histologic evidence of so-called probable beginning cancer. Obviously no such incidence would occur in an unselected group of women who were similarly examined.

## COMMENT

One cannot escape the feeling that there is considerable partisanship and bias on the part of the proponents of the colposcope. In fact one sees the question raised, in some of the discussions, of the advisability of enacting legislation compelling physicians who examine patients under the existing German sickness insurance plans to use the colposcope in all vaginal examinations.

The impression is unescapable that for the present the recognition of cancer of the cervix uteri in its early stages still rests on painstaking visualization and inspection and proper obtainment from unusual appearing areas of tissue for microscopic examination. To await the appearance of a large ulcer formation, obvious induration or a cauliflower-like tumefaction such as that described in textbooks before clinically suspecting cancer is like preparing for sea after the ship has sailed.

This critical evaluation of methods more or less recently popularized for the apparent simplification and ready determination of early cervical cancer should not be construed as unfriendly criticism. However, as noted before, on the basis of a fairly long and appreciable experience I believe that these methods possess greater limitations than is ordinarily ascribed to them. If these restrictions are appreciated, one will not be discouraged by finding little where much was anticipated.

808 Medical Dental Building.

13. Hinselmann, H.: Die Grundlagen der kolposkopischen Karzinombekämpfung, *Zentralbl. f. Gynäk.* 58: 2798 (Nov. 24) 1934.

14. Mestwerdt, Gustav: Zur Frage der Diagnose des latenten Portiokarzinoms, *Zentralbl. f. Gynäk.* 61: 2742 (Nov. 27) 1937.

15. Mönkeberg, Agnete: Auch ein Anfänger kann das Portiokarzinom im ersten Beginn mit dem Kolposcop entdecken, *Zentralbl. f. Gynäk.* 62: 52 (Jan. 1) 1938.

16. Leip, F., und Otto, Karl: Ein Portiokarzinom, entstanden aus einer 12 Jahre lang beobachteten Leukoplakie, *Zentralbl. f. Gynäk.* 61: 242, 1937.

17. Hinselmann, H., and Köhler: 3½ Jahre "Krebsprechstunde" mit dem Kolposkop, München. med. Wchnschr. 54: 1082 (July 9) 1937.

## Council on Industrial Health

### ETIOLOGY OF PNEUMOCONIOSIS

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*This paper is one of a series on pneumoconiosis prepared at the request of the Council on Industrial Health. The succeeding articles will be published when available.—Ed.*

Although the term pneumoconiosis was not introduced until the nineteenth century, clinical symptoms were naturally enough associated with the inhalation of dust in occupation by the earliest medical writers. In the Renaissance both physicians and mining engineers were well aware of the fact that the metal miner suffered from shortness of breath and died prematurely, and anatomists had described "heaps of sand" in the lungs of stone cutters which grated on their knives. They called the condition phthisis, their term for any chronic disease of the lungs which was associated with emaciation and expectoration. While most of the various conditions originally known by this name were differentiated and fully described in the eighteenth and nineteenth centuries, it was not until 1902 that the role of inhaled dust began to be understood. In that year an English departmental committee, of which Dr. J. S. Haldane was the outstanding member, pointed out that the phthisis from which the Cornish tin miners suffered was different from ordinary tuberculosis. They concluded that "the primary injury of the lungs is due solely to the inhalation of stone dust but that this injury, while it is apparently capable of gradually producing by itself great impairment of respiratory functions . . . also predisposes enormously to tuberculosis of the lungs, so that a large proportion of the miners die from tubercular phthisis."

A few years later, in 1915, Collis<sup>1</sup> demonstrated that not all kinds of dust had the same effect. His statistical analyses of morbidity and mortality in workmen in various dusty trades indicated most clearly that exposure only to free silica dust was particularly dangerous. Such exposure caused disability with ultimate death from tuberculosis at an age period later than occurred in the rest of the population. Inhalation of silica combined as silicates or of nonsiliceous dusts had no such effects. Collis felt very strongly that the free silica particles did not injure the lungs by virtue of their hardness and sharpness because other particles with the same properties failed to do so, but he could offer no other explanation. In 1922 Gye, Kettle and Purdy<sup>2</sup> demonstrated that colloidal silica is toxic for rabbits and suggested that crystalline silica is dissolved in the body to produce the toxic colloid. These contributions of Collis and of Gye, Kettle and Purdy still dominate modern concepts of pneumoconiosis.

Clinical research in South Africa under the leadership of Watkins-Pitchford and Irvine clarified the relationships existing between the reaction to inhaled silica and tuberculous infection. By employing the method of serial roentgenography over long periods of time and checking their observations with post-

From the Saranac Laboratory for the Study of Tuberculosis of the Edward L. Trudeau Foundation.

1. Collis, E. L.: Industrial Pneumoconiosis, with Especial Reference to Dust Phthisis, *Milroy Lectures*, 1915, *Pub. Health* 25: 252-292, 1915.

2. Gye, W. E., and Purdy, E. H.: The Poisonous Properties of Colloidal Silica, *Brit. J. Exper. Path.* 3: 75-85 (April) 1922. Gye, W. E., and Kettle, E. H.: Silicosis and Miners' Phthisis, *ibid.* 3: 241-251 (Oct.) 1922.

mortem examinations these observers have probably contributed more than any other group to a sound understanding of the pathogenesis and pathology of silicosis. Their work established the dual relationship existing between the infectious process tuberculosis and silicotic fibrosis. The infection may on the one hand remain latent and exert only an etiologic effect in modifying the amount and form of the reaction to silica dust; on the other it may itself develop in active but unusually chronic form as a result of the preestablished silicosis.

Until 1924 Collis's dictum that only free silica is a cause of pulmonary fibrosis remained unchallenged. In that year Cooke<sup>3</sup> reported a case in which inhaled asbestos was incriminated; other cases were soon discovered and today asbestosis is everywhere recognized as a second form of pneumoconiosis characterized by fibrosis. The disease can apparently be produced by the prolonged inhalation of any of the five different silicates known as asbestos. This form of pneumoconiosis does not seem to predispose to tuberculosis to the same degree as silicosis. Although English authorities believe that it has considerable effect, American experience has failed to reveal an excess of tuberculosis among asbestos workers.

A few years later Badham<sup>4</sup> reported peculiar conditions found on roentgen examination in a large group of gold miners in Western Australia. These men had been exposed to a dust containing a small amount of quartz mixed with a silicate of magnesium known as rhodonite. Since Badham's films bore a certain resemblance to those showing asbestosis and to those of men exposed to various other silicate dusts, he proposed the term "silicatosis" to describe all these conditions. His proposal has not been generally accepted as proof that the silicates as a class can produce fibrosis.

Today Collis's clearly defined concepts of pneumoconiosis are becoming confused again because enthusiastic observers in many fields are drawing deductions without sufficient knowledge of the problem as a whole. Roentgenologists are too ready to ascribe any abnormal shadow in the film of a workman to some dust which he may have inhaled. General pathologists have concluded that the mere presence of a certain mineral in a pulmonary lesion is *ipso facto* proof that this dust was the cause of the reaction. Experimental pathologists with high powered microscopes have searched the early reactions to inhaled dusts and drawn sweeping conclusions as to the potentialities of this or that mineral to cause fibrosis. Petrologists and chemists are performing test tube experiments which prove that some silicate is more soluble in water than quartz, deducing from the solubility hypothesis that it must therefore be a more potent irritant than quartz. Clinicians, who see only the disabled silicotic patient with advanced lesions, often complicated by tuberculosis, are insisting that only such conditions represent the true picture of silicosis.

Such intensive research on the different aspects of the problem is yielding valuable information, but theoretical knowledge is not yet sufficiently advanced to permit an evaluation of a hazard by mere analysis of dust or rock. At the present time the detailed study of the workman and his industrial environment still

constitutes the only certain method of establishing the existence of a dust hazard. Such investigations are profitably based on the experience of the Miners' Phthisis Prevention Committee in South Africa. They should include the following:

1. The occupational history of all employees should cover the entire industrial life of every workman. It should include the names of each employer, the kind of job, an estimate of the type and quantity of dust encountered and the approximate dates of each position held. The information is apt to be recalled most readily in reverse chronological order.

2. Roentgenologic examination of the chest constitutes the most important source of information as to the presence of abnormal changes in the lungs. For the detection of advanced lesions almost any quality of roentgenogram on film or paper will suffice; to discover early changes the best stereoroentgenograms are none too good. The interpretation of the films presupposes a thorough knowledge of the normal pulmonary patterns, a familiarity with the shadows of infectious lesions, and judgment unbiased by the knowledge that the subject may have been exposed to considerable dust.

3. Physical examination of the chest is of equal significance. In many cases in which films may reveal widespread pneumoconiosis, even of a silicotic type, the physical signs will be very slight, but this paradox in itself is significant. Complicating infections are usually productive of characteristic signs but they are often less obvious than in cases of simple infection. Only by physical examination is it possible to evaluate the effect of the pulmonary condition and determine whether disability exists.

To be most profitable, such examinations should be repeated at intervals, annually if possible and on infected individuals as often as the examining physician deems necessary. By serial reexamination of a considerable group it is possible to obtain an idea of the pathogenesis of a pneumoconiosis, its rate of development and its extent and probable outcome. Isolated examinations, not repeated, demonstrate the prevalence of abnormal changes in the lungs of the workmen. Little information as to evolution of disease can be obtained for the conditions of exposure in the present, and previous employment varies with the individual workman.

4. Postmortem examination of the lungs should be made as frequently as possible. Careful gross and histologic study of the pulmonary lesions constitutes the best guide to the interpretation of the shadows which are cast on a roentgenogram. Chemical and petrographic analysis of the lungs determine the amount and character of the inhaled mineral dust. The larger the number of such postmortem examinations the greater the likelihood of formulating a true concept of the disease arising from the dust under investigation. One or two isolated examinations may only obscure the picture because of previous exposures to other dusts not accounted for in the occupational history.

5. A detailed study of the industrial environment includes a chemical and petrographic analysis of the raw materials, in the case of a mine of the ore and the rock being worked, of a grinding operation of the wheels and the implements ground, and so on. But it should not be assumed that the composition of the raw materials will necessarily correspond with that of the dust created by manipulating them. It will be shown later that the free silica content of the rock may greatly exceed that of the dust liberated from it. Likewise, samples of dust settled on rafters do not necessarily contain the same proportion of silica as the dust suspended in the atmosphere. Analysis of air-floating material at the breathing level constitutes the only accurate measure of the dangerous minerals that a workman is likely to inhale. The relative amounts of silica and all other minerals should be determined because of mutual interactions which may reduce the concentration of the silica or modify its effects on the body. Not only the kind but

3. Cooke, W. E.: Fibrosis of the Lungs Due to the Inhalation of Asbestos Dust, Brit. M. J. 2: 147 (July 26) 1924.

4. Badham, C.: Notes on a Fine Type of Fibrous Pneumoconiosis Produced by Silicates and Other Minerals, Report of Director-General of Public Health (New South Wales) for year ended Dec. 31, 1927, Sydney, Australia, Government Printing Office, 1929.

the quantity of the atmospheric dust must be measured. In the United States the Greenburg-Smith impinger apparatus is the standard, and the results are expressed in millions of particles per cubic foot of air. Other instruments, such as the Kotze konimeter used in South Africa, the Owens jet counter in Great Britain and the Bausch and Lomb dust counter in this country, give equally satisfactory results but ones which are not reciprocally translatable.

Such determinations must be made in all the various parts of the plant or mine where men are at work, for both the quantity and the quality of the dust vary from the point of generation to others more remote. Furthermore, repeated sampling is essential to establish the amount of dust that the men inhale in any operation. Local variations in the velocity of air, humidity and general ventilation all affect the picture. The average amount of atmospheric dust must be based on many samples taken over periods of months or years.

By correlating the results obtained from such a study it is possible to evaluate the effects of the particular dust under the conditions existing in a particular plant. The results can be applied to another industry only when it has been proved that the composition and concentrations of dust in the second plant are similar. Only then is it safe to assume that the mass effects will be comparable. Individual variations will always be discovered because certain persons are more susceptible to dust by virtue of associated pulmonary infections. Sometimes the picture in the whole group will be altered because of a high local incidence of tuberculosis.

#### EXPERIMENTAL INVESTIGATIONS

Since so many industrial processes involve creation of dust and since a detailed study of each one of them would be both time consuming and expensive, there is reason to seek accessory sources of information. Animal experimentation has demonstrated its value as such a source. While many experiments have failed to reproduce disease processes entirely comparable to those observed in human beings, they have demonstrated fundamental principles which govern the reaction of living tissues to various kinds of mineral particles.

The experimental pathologist may test the action of a given dust by the inhalation method, which purports to create an atmospheric environment comparable to that in industry. This method is time consuming, expensive and fraught with technical difficulties, and frequently it fails to produce the anticipated results. The experimenter sets up rigidly controlled conditions, which are kept as constant as possible over periods of months or years; in industry conditions are rarely constant but continue to change from hour to hour. With pure mineral dusts experimental inhalation generally produces a pneumoconiosis comparable to that in human beings. With dusts composed of mixtures of silica and other minerals the results are often disappointing even when the dust being tested is the apparent cause of human disease. Failure may be due to the time limitation imposed by the span of life of the ordinary laboratory animals or by the failure to appreciate and reproduce the complex factors of industrial exposure. Nevertheless the inhalation method may lead to an appreciation of these factors; it is establishing the conditions which govern the behavior of atmospheric suspensions of dust particles and those which determine inhalation into the lungs. It is elucidating the pathogenesis of various pneumoconioses in normal and in infected lungs.

By injection methods the experimenter may demonstrate the potentialities of any type of mineral to irritate

living tissues and may determine the character of the response. He must avoid technics which produce confusing nonspecific effects due to local trauma and the mere mechanical action of large amounts of any foreign body. This objection can be overcome by injecting dilute suspensions of particles at points remote from the site of ultimate localization. I prefer repeated intravenous injections of dilute suspensions of particles which permit gradual accumulation of the test substance in different organs. I have also employed the Miller-Sayers<sup>5</sup> intraperitoneal method; this gives good gross reactions but the microscopic pictures are hard to evaluate. Experiments with intratesticular injections are also in progress and may prove useful.

Since the objective is the determination of the capacity of a mineral to cause fibrosis, it generally makes very little difference whether its action is tested in the lung or in some other organ. Fibrous tissue develops from continued stimulation of connective tissue cells regardless of their location. As far as is known, these elements are just as capable of stimulation in the spleen or liver as in the lungs. In the case of free silica, this assumption has been proved beyond question, and furthermore it has been shown to hold good in any species of animal tested. The only apparent exceptions thus far discovered have been the fibrous minerals known as asbestos, which have produced little or no scar tissue outside the lungs. Reasons will be cited for suspecting that the fibrosis of asbestosis is due to mechanical irritation which is restricted to the lungs because of the active motion of this organ. In other locations the factor of rapid and continuous motion is lacking.

The etiology of the pneumoconioses will be discussed first from the point of view of the capacity of different minerals to irritate the tissues; the factors that govern the behavior of air-borne dust will then be considered, and finally the host factors that determine the amount of dust inhaled and modify the cellular reactions. For this consideration the minerals will be classified into groups consisting of free silica, combined silica, non-siliceous particles and mixtures composed of free silica and other substances.

A recent paper<sup>6</sup> reported uncompleted results of injections of physiologic solution of sodium chloride suspensions of different mineral particles into animals. These are summarized in tables taken from that publication but brought up to date when longer periods of observation have supervened. The capacity of different mineral particles of the same size and concentration to irritate the tissues is indicated by a series of numerals and plus signs. The significance of these symbols is indicated by the following definitions:

± Simple phagocytosis, often by giant cells, without other cellular reaction; no fibrosis.

+ Phagocytosis plus small localized collections of lymphocytes; reaction nonprogressive; no fibrosis.

2+ Similar to + but with more extensive infiltration of lymphoid cells; reaction nonprogressive; no fibrosis.

3+ Early proliferation of mononuclear cells, localized to immediate vicinity of primary phagocytes with further evidence of chronic inflammation. If any elements of fibrosis appear they are microscopic in extent and nonprogressive in character.

5. Miller, J. W., and Sayers, R. R.: The Physiological Response of the Peritoneal Tissue to Dusts Introduced as Foreign Bodies. *Pub. Health Rep.* 49: 80-89 (Jan. 19) 1934.

6. Gardner, L. U.: Reaction of the Living Body to Different Types of Mineral Dusts With and Without Complicating Infection. *Mining Technology*, May 1938.



4+ More extensive proliferation followed by fibrosis suggestive of early silicosis but not progressing to the mature hyaline stage.

5+ Typical, nodular, silicotic fibrosis, hyaline in character and progressive in type; the standard reaction.

6+ and 7+ Progressive fibrosis, hyaline in character but diffuse rather than nodular in form; observed only with two synthetic forms of free silica, cristobalite and tridymite.

8+ Acute toxic reactions with local necrosis of cells often resulting in death of the animal; little fibrosis in event of survival.

#### FREE SILICA

Table 1 sets forth the forms of free silica which have been tested by intravenous injection of 1 Gm. of particles of from 1 to 3 microns in diameter into the ear veins of rabbits and by other methods. The maximum period of observation in all cases has been eighteen or twenty-four months.

It will be noted that all the crystalline and crypto-crystalline forms of free silica are as active as or more active than the standard normal quartz. All of them have also produced progressive fibrosis of a silicotic type in guinea pigs, rabbits and white rats and in some cases other species. These results indicate that all the forms of free silica enumerated are capable of producing a progressive fibrosis if effective quantities remain in contact with living connective tissue. They

TABLE 1.—Free Silica

Crystalline Forms		Cryptocrystalline Forms		Amorphous Forms	
Normal quartz.....	5+	Chalcedony.....	5+	Colloidal silica, dispersed.....	8+
Tridymite.....	7+	Trippoli (Seneca, Mo.)	5+	Colloidal silica, gel ±	
Cristobalite.....	6+	Flint.....	5+	Opal.....	4+
Vitreous silica.....	5+			Diatomite.....	5+

prove nothing as to the capacity of these forms of silica to remain suspended in the atmosphere and to be inhaled in dangerous quantities.

The observations on the amorphous varieties of free silica are more variable. Colloidal silica in a dispersed phase is exceedingly irritating and in too large an intravenous dose it causes almost immediate death. If the same suspension is allowed to gel either spontaneously or by changing its reaction, the silica promptly loses its irritating properties. The finely ground particles of the gel are phagocytosed by mononuclear cells, which subsequently develop epithelioid characteristics and often form giant cells of the Langhans type.<sup>7</sup> But with these transformations in the primary phagocyte, the manifestations of irritation cease; there is not even a local infiltration with lymphocytes to suggest any effect on the surrounding tissues. The picture has remained unchanged over a two year period; if anything the number of giant phagocytes has been less in animals killed two years after injection than in one killed at three months.

The natural minerals composed of amorphous silica, like opal and diatomaceous earth, are much more active. Pure diatomite produced a reaction which was indistinguishable from that to quartz, while opal caused a nonhyaline fibrosis which was atypical and which had begun to retrogress after a period of one year. In an attempt to explain this puzzling difference in the irritating properties of different forms of free amorphous silica, supplementary tests are being made with synthetic gels of variable water content. Eight months

after injection into the peritoneal cavities of guinea pigs not one of the six compounds has produced any appreciable fibrosis. The factor of water content can in all probability be eliminated. The desirability of testing other natural forms of amorphous silica is obvious.

Further supplementary tests have revealed pertinent facts with regard to the behavior of normal quartz and the other crystalline forms. The factor of dosage will be of more importance when the effects of mixed dusts are discussed. For pure, free, active silica the dose employed in all these tests has been excessive. As little as 0.05 Gm. of normal quartz will cause as much reaction as 1 Gm. in a 5 pound (2.3 Kg.) rabbit, but two years instead of one is required for mature reaction. A dose of 0.01 Gm. causes no visceral fibrosis, but the lymph nodes are still involved (the result of lymphatic drainage). Nevertheless the 1 Gm. dose has been used for the comparative study to insure the presence of adequate quantities of minerals that may be less irritating than quartz.

The rate and extent of tissue reaction are inversely proportional to particle size.<sup>8</sup> When the quartz is larger than 10 microns in diameter, reaction does not progress appreciably during a two year period of observation. Particles less than 1 micron in diameter cause increasingly acute inflammatory responses and often death from hepatic insufficiency within a few months. However, the size can be reduced to a point such that the particles are no longer retained in most parts of the body, and then their effect is again negligible. Intravenous injection of 1 Gm. of active vitreous silica particles with a maximum diameter of 0.002 micron produced no symptoms, but excessive amounts of silica were present in the urine. All the animals survived and when they were killed showed only minute foci of silicotic fibrosis.

Inhalation tests were also attempted with this fine dust to determine whether appreciable quantities would be retained in the lungs. The exposure to an undefined concentration of this very fine dust was continued for eight hours daily over a period of five months. At the end of this period pneumonia was making heavy inroads into the group, probably because of overcrowding in too small a dusting chamber. When the survivors were killed their lungs showed no fibrosis, but giant cells of the Langhans type were even more numerous than with larger quartz. It was concluded that some of the fine silica was retained, but in the absence of a method of measuring the atmospheric concentration the amount could not be estimated.

#### SILICATES

In a similar manner a group of representative silicates, most of which are used in industry, are being subjected to tests by animal injection. Table 2 summarizes the results as far as the observations have progressed. Not included in the table is a series of tests on synthetic sodium silicate. This substance is exceedingly toxic when the standard dose of 200 mg. is injected into the peritoneal cavity of guinea pigs. The animals die within a few minutes, exhibiting symptoms of silicic acid poisoning. Presumably its ready solubility is responsible for the toxicity of this silicate. Incidentally, repeated injections of minute quantities of the same substance into the lungs have

7. Gardner, L. U.: The Similarity of the Lesions Produced by Silica and by the Tubercle Bacillus, *Am. J. Path.* 13: 13-23 (Jan.) 1937.

8. Gardner, L. U., and Cummings, D. E.: Reaction to Fine and Medium Sized Quartz and Aluminum Oxide Particles: Silicotic Cirrhosis of the Liver, *Am. J. Path. (supp.)* 9: 751-763, 1933.



caused neither symptoms nor fibrosis, so that it seems fair to conclude that any quantity of sodium silicate which could be inhaled would be harmless.

As far as these observations have progressed, none of the silicates have proved capable of producing a fibrous type of reaction. Some of them, marked "(d)" in the table, have caused sudden deaths on intravenous injection into rabbits. Such reactions, owing either to mechanical occlusion of the blood vessels or to the toxic action of silicic acid formed in the preparation of the dust suspensions, probably have little to do with the subject under discussion. Beryl is apparently toxic and produces acute local inflammation that invariably leads to death. A few of the silicates, notably biotite mica and some of the clays, have provoked local proliferation of mononuclear phagocytes. Whether this early reaction will ultimately end in fibrosis awaits demonstration. If fibrosis should develop it will do so only after much longer contact with the tissues than is required in the case of free silica. Most of the silicates have excited an inert foreign body type of tissue response consisting of simple phagocytosis and giant cell formation with or without lymphocytic infiltration. Such reactions either have remained unchanged for periods of one or two years or have tended to retrogress. It is of interest to note that fibrous sericite of the type which Jones<sup>9</sup> stated might be such an important adjunct in the production of silicosis is among the most inert of the silicates.

Since the first publication on the action of silicates<sup>6</sup> the results of a few tests by still other methods have become available, which suggests that these tentative conclusions may need revision. When 5 mg. of suspensions of several different minerals was injected directly into the testes of guinea pigs it was found that the same feldspar produced a very active cellular proliferation within six months. Talc produced a less active response of a similar character. Garnet, sillimanite and platy sericite behaved in just the same manner as they did in the tests previously reported. The intratesticular injections involved excessive local concentrations, but the marked difference between the response to several silicates by this method and by the others employed suggests the necessity for further study. Possibly other silicates besides feldspar and talc will cause more reaction when sufficient quantities are thus concentrated in one small area. Time must demonstrate whether the initial change will progress to fibrosis. However, the practical significance of such massive doses remains doubtful.

#### ASBESTOS

The asbestos group of silicates, including anthophyllite, amosite, amphibole, crocidolite and chrysotile, have invariably failed to cause fibrosis or even early proliferation either intravenously in rabbits or in the peritoneal cavity of guinea pigs. Miller and Sayers<sup>5</sup> had a similar experience with three forms, chrysotile, amosite and crocidolite, and they classified them as inert substances. Obviously these observations are at variance with the well recognized capacity of asbestos to produce fibrosis of the lungs and demand explanation. One should not be too ready to condemn the method or to conclude that animals are incapable of reacting to asbestos. The method has worked consistently with free silica, and extensive pulmonary fibrosis has devel-

oped in guinea pigs when made to inhale chrysotile fibers. It is felt that the failure of these fibrous silicates to produce fibrosis in organs outside the lungs has real significance.

A very considerable number of observations are pointing to the hypothesis that the fibrous silicates behave in a different manner from the particulate minerals and that they irritate the lungs mechanically. Unlike quartz and the other active free silicas, not only have they failed to produce fibrosis in organs other than the lungs but they have not become more irritating as particle size decreases. Chrysotile fibers less than 3 microns in length are no more active than the silicate serpentine, which has the same chemical composition but is massive rather than fibrous in structure. Even by inhalation chrysotile, ground to such

TABLE 2.—Combined Silica or Silicates

Group	Variety	Rabbit's Vein		Guinea Pig's Peritoneum	
		Maximum Period Observed, Months	Tissue Reaction	Maximum Period Observed, Months	Tissue Reaction
Feldspar	Na-Microcline.....	24	±	12	+
Pyroxene	Rhodonite.....	5	3+	4	+
Amphibole	Anthophyllite.....	12	+	12	+
	Amosite (fibrous).....	6	+++	4	+
	Na-Tremolite.....	12	+++	12	++
	Amphibole.....	6	+++	12	+
	Crocidolite.....	12	+++	12	++
	Beryl.....	3½	2+(d)	4	+
Garnet	Almandite?.....	24	±	12	±
Topaz	Sillimanite.....	24	±	12	±
Zeolite	Analcite.....	24	±	12	+
Mica	Muscovite.....	6	2+	4	2+
	Sericite (fibrous).....	21	+	12	++
	Sericite (platy).....	24	+(d)	12	++
	Biotite.....	4½	3+(d)	8	+
Serpentine	Serpentine.....	12	±	12	±
	Chrysotile (asbestos).....	9	+(d)	12	+
Talc	Talc.....	24	2+	12	2+
	Glauconite.....	12	+(d)	12	+
Kaolin	Dickite.....	6	2+	4	2+
	Halloysite.....	4	3+	4	2+
	Montmorillonite.....	3	2+	8	2+
Titanosilicates	Titanite.....	6	±	4	2+

d = sudden death.

fineness that its fibrous structure is no longer recognizable, has produced no suggestion of fibrosis after a year's exposure. If its action were chemical, the reduction in particle size should have resulted in an accelerated tissue response. The fibrosis of asbestosis that occurs in the lungs is not characterized by the hyaline transformation characteristic of the chemical action of free silica. In experimental animals, at least, the fibrosis of pulmonary asbestosis does not progress after exposure to the dust is discontinued, as invariably happens with free silica. All these observations suggest a mechanical rather than a chemical form of irritation. It has been inferred that reaction to asbestos is restricted to the lungs because only these organs possess the proper structure and physiologic activity to permit friction with a stiff fibrous foreign body.

The most obvious objection to this hypothesis is concerned with the formation of that peculiar structure known as the asbestosis body. It is produced by a thick coating of iron and probably organic material laid down on the surface of an asbestos fiber. The deposit

9. Jones, W. R.: Silicotic Lungs: The Minerals They Contain, J. Hyg. 33: 308-329 (Aug.) 1933.

is extremely irregular in outline with terminal globular swellings and numerous transverse haustrations. It is a golden yellow and, like the blood pigment hematin, it gives microchemical reactions to iron. In the lungs of guinea pigs, asbestos fibers must remain in contact with the tissues for about two months before the coating becomes recognizable. Asbestosis bodies also occur in man and have been reported in the lungs of brown rats.<sup>10</sup> In the lungs of cats, rabbits and white rats subjected to prolonged inhalation of asbestos dust they have never been discovered. In other organs they usually fail to develop; only in very rare instances have one or two bodies been detected in the peritoneal cavities of guinea pigs injected locally. They are reported as absent in the "asbestos corns" which appear on the hands of workmen handling this fibrous mineral.

The absence of asbestosis bodies in tissues other than the lungs suggests that chemical changes peculiar to that organ are responsible for their development. Since

tions of the first three to six months will be followed by fibrosis. Other silicates of a fibrous structure may act as mechanical irritants in organs with appropriate architecture and functional activity.

#### SILICON CARBIDE

One compound of silicon, which is not a silicate but a carbide, deserves special mention because it has such widespread industrial use as an abrasive. It is known to commerce by various trade names such as "carborundum" and "crystolon." By any of the injection methods it has failed to cause even a suggestion of fibrosis. The particles are phagocytosed by cells which merely enlarge to accommodate the foreign bodies in their cytoplasm without the "epithelioid" alterations suggestive of slight toxicity. There has been no change in the original picture within a period of two years after the injection of the standard doses. In the scheme employed throughout this work the reaction to silicon carbide has been classified as  $\pm$ . After inhalation for a period of two and one-half years the lungs show excessive focal accumulations of dust associated with slight degrees of chronic inflammation. The lack of fibrosis following the injection of particles of this exceedingly hard abrasive constitutes very good evidence for rejecting the properties of hardness and sharpness as a cause of such reaction.

#### NONSILICEOUS MINERALS

Similar tests have been performed with a number of pure minerals containing no silica. As indicated in table 3, none of them have caused primary fibrosis; a few have provoked slight chronic inflammatory reactions; some have been toxic. With large doses selected as standard, the "toxic" minerals have either caused immediate death (e.g., dolomite) or excited acute inflammations the healing of which resulted in scar formation. The response to massive doses of toxic substances, such as the sulfides, has no bearing on the subject of pneumoconiosis, in which the quantities inhaled could never approximate those used for injections.

Aside from the toxic reactions that healed with the formation of more or less scar tissue, none of these nonsiliceous dusts have produced any fibrosis. Diamond, the hardest known mineral, and aluminum oxide, a common abrasive in industry, are inert. Soft coal is slightly more irritating than anthracite. The reaction to the satin spar form of gypsum will in all probability prove to be quite inert when the tests are completed. It so happened that the last animal of the series to be killed showed somewhat more chronic inflammation than other members of the series, so that its effect is noted as "2 + ?" in the table.

#### MIXTURES OF FREE SILICA WITH OTHER MINERALS

Apparently there are certain substances capable of depressing the action of silica, and there may be others which accelerate it. As long ago as 1918 Haldane<sup>12</sup> expressed the belief that coal dust inhaled at the same time as silica prevented the development of silicosis. His belief was based on clinical statistics and on experiments performed by Mavrogordato.<sup>13</sup> By 1929 the latter seems to have lost faith in these observations, for he wrote "The presence of carbon in the air does not

TABLE 3.—Nonsiliceous Minerals

Mineral	Injections of						Other Tests	Type of Test
	Rabbits		Guinea Pigs					
	Maxi- mum Time Obs- served, Months	Tis- sue Obs- served, Reaction Months	Maxi- mum Time Obs- served, Months	Tis- sue Obs- served, Reaction Months	Maxi- mum Time Obs- served, Months	Tis- sue Obs- served, Reaction Months		
Diamond.....	36	±	..	..	..	..	..	..
Coal, bituminous.....	12	2+	12	±	41	±	Inhaled	..
Coal, anthracite (1.76% SiO <sub>2</sub> ).....	12	±	12	±	12	0	Subcutaneous	..
Silicon.....	..	..	..	..	5	±	Subcutaneous	..
Aluminum oxide.....	24	±	12	±	12	±	Subcutaneous	..
Rutile.....	..	..	11	±	11	±	Subcutaneous	..
Marble.....	..	..	1	0	3	0	Subcutaneous	..
Gypsum, satin spar.....	12	2+?	..	..	..	..	..	..
Gypsum, calcined*.....	..	..	5½	2+	24	±	Inhaled	..
Galena.....	..	..	12	(Calcif.) Abscess and repair	..	..	..	..
Chalcopyrite.....	..	..	12	±	..	..	..	..
Iron sulfide.....	..	..	12	±	..	..	..	..
Zinc sulfate (roasted sulfide ore)	11	2+	12	Abscess and repair	..	..	..	..
Fluorite (0.8% SiO <sub>2</sub> )...	18	2+	11	2+	..	..	..	..
Dolomite.....	1½	Death	0	Death	..	..	..	..

\* In the original publication\* calcined gypsum was erroneously reported to have produced no reaction six months after injection into the ear veins of rabbits. This dust has not been tested by the intravenous method.

a fibrous reaction has been observed only in the tissues where the bodies have been numerous,<sup>11</sup> the question arises as to whether the chemical changes responsible for the deposit on the mineral fiber is the same one that affects the tissues of the host. No answer is yet available, but it is quite conceivable that the two effects are independent of each other. It has been suggested that the irritated tissues attempt to protect themselves by laying down the coating, and as a matter of observation subcutaneous injection of asbestosis bodies recovered by digesting human lung tissue with antiformalin has caused no fibrosis in guinea pigs.

These observations would suggest that as a class the silicate minerals are not irritating because they contain silica, which is liberated by chemical action of body fluids. A few of them, like biotite mica, beryl and some of the kaolins, seem to have essential molecular structures capable of provoking acute inflammation or early proliferation. Their action has not been followed long enough to demonstrate whether these early reac-

10. Gloyne, S. R.: The Morbid Anatomy and Histology of Asbestosis, *Tubercle* 14: 550-558 (Sept.) 1933.

11. The human cutaneous lesions may constitute an exception but there is some question as to the exact structure of these lesions.

12. Haldane, J. S.: Dust Inhalation in Mines: Effects on Health, *Scientific Am. (Supp. 2225)*, Aug. 24, 1918, p. 119.

13. Mavrogordato, A.: The Etiology of Silicosis, *Réunion de la Commission internationale permanente pour les maladies professionnelles*, Lyons, April 3-6, 1929.

appear to affect the changes produced by silica other than coloring them." Apparently most clinical observers also gave up the Haldane theory of a protective action by coal dust after several years.

Recently, however, experimental pathologists have renewed their interest in the idea. I have long been impressed by two observations; it is not at all difficult to produce nodular fibrosis by making small laboratory animals inhale relatively pure, free silica, but they do not react in a similar manner to mixed dusts in which the silica is associated with considerable amounts of other minerals. Prolonged inhalations of heavy concentrations of natural mixtures such as granite and ferruginous chert or of artificial mixtures composed of fine quartz and gypsum dust have not produced an effect commensurate with the quantity of silica available in the atmosphere. Rather than condemn the inadequacy of the experimental method, I have attempted to discover whether there are reasons for the apparent failures.

Injectations indicate that the presence of various other minerals in a mixture may retard the usual reaction to silica, restricting the extent of tissue involvement and modifying the form of the cellular response. Different classes of minerals seem to be capable of acting in this manner. Some of them occur in natural combination with free silica; others have been added artificially. Not enough is known about inhibitors to evaluate their effects quantitatively or to attempt to classify them, but their action is sufficiently striking to deserve more than passing mention.

Table 4 summarizes the experience in a long series of experiments based on injection and on inhalation of mixtures of some form of active silica and other minerals. The table indicates that injection produces much more reaction than exposure by inhalation to a dust of the same composition. Even on injection, however, the response to a given quantity of silica is modified. Both the rate at which reaction develops and its intensity are affected. Quite naturally the modification is most marked in cases in which nonsiliceous elements are found in excess.

Table 4 indicates that a variety of minerals may inhibit the action of quartz in the body: iron oxide, coal and some constituent of granite, probably the silicates (feldspar or mica), but perhaps some other element present in smaller amounts. The series would suggest that inhibition is most effective in the presence of small amounts of silica. The experience with anthracite coal and crude fluorite which are contaminated with practically the same quantities of silica implies that not all inhibitors are equally potent. The reactions to the different doses of granite and chert are indicative of the relative importance of the two factors dosage and time. In the various tests on these two minerals, from three to ten times the quantity of silica necessary to produce marked progressive fibrosis has been injected, but in the presence of inhibitors cellular reaction has been delayed. In the case of granite, mature fibrosis has never appeared, and even after twenty-two months the cellular picture is the same as that produced by the quartz alone in one or two months. In chert the proportion of silica to iron oxide is higher, and hence it should not be concluded that iron is a less effective inhibitor.

The consistent results observed in all animals used to test this series of minerals containing increasing proportions of free silica makes it seem most probable that the principle of inhibition is a valid one. The mecha-

nism by which inhibitors exert their effects has yet to be demonstrated. The bearing on the general problem of etiology is obvious, for one must conclude that the rate and severity of reaction do not depend solely on the amount of free silica in the mixture. They are inversely affected by the other components of the dust.

The dust from the South African gold mine contained 70 per cent of quartz and yet even in this proportion the silica is somewhat inhibited. Reaction developed slowly, and after sixteen months the silicotic lesions were less advanced than those of the pure quartz standard. Incidentally the sericite, which with platy muscovite and a trace of feldspar and possibly ilemite make up the remaining 30 per cent of this mixture, has failed to accelerate the action of the quartz as Jones hypothesized. Experimentally it has not itself caused fibrosis nor has it accentuated the effect of free silica.

There still remains for consideration the evidence which has been interpreted as indicative of accelerator

TABLE 4.—*Mixtures of Silica and Other Substances*

Mineral and Silica Content	Rabbits		Guinea Pigs		Other Tests	
	Maxi- mum Period Ob- served, Months	Tis- sue Reac- tion	Maxi- mum Period Ob- served, Months	Tis- sue Reac- tion	Maxi- mum Period Ob- served, Months	Tis- sue Reac- tion
Hematite (6% SiO <sub>2</sub> ).....	12	±	12	+	48+8*	+
Anthracite (10.13% SiO <sub>2</sub> )....	12	±	12	+	21	0
						Subcu- taneous
Crude fluorite (10.39% SiO <sub>2</sub> )	12 15½	3+ 4+	11	2+	11	±†
						Inhaled
Granite (35% SiO <sub>2</sub> )						
Usual dose=0.3 Gm. SiO <sub>2</sub> ..	12	2+	12	+	30	2+†
	15	3+				
3 times usual dose=1 Gm. SiO <sub>2</sub>	12 22	2+ 3+	..	..	..	..
						.....
Ferruginous chert (50% SiO <sub>2</sub> )						
Usual dose=0.5 Gm. SiO <sub>2</sub> ..	12	4+	12	3+	22½+26*	+
	19	5+	12	3+		
Twice usual dose 1 Gm. SiO <sub>2</sub>	12	5+	..	..	..	..
						.....
South African mine dust (70% SiO <sub>2</sub> )	16	4+	12	3+	..	..
						.....

\*Forty-two months in the dusting room plus eight months in a normal atmosphere and similarly twenty-two and one-half months in the dusting room plus twenty-six months in a normal atmosphere.

† In one or two animals nodular fibrosis (4+) developed in the lymph nodes draining the lungs but pulmonary fibrosis was lacking.

substances. The matter came to light in the examination of a few persons engaged in the manufacture of soap powders who died after exposures of a few months or years. The first cases were reported by MacDonald, Piggot and Gilder<sup>14</sup> in England, and subsequently a few more were found by Chapman<sup>15</sup> and others in this country. It was shown that the soap powder contained large amounts of very fine silica and appreciable quantities of free alkali. On the basis of the solubility hypothesis it was postulated that unusual quantities of silica had dissolved in the alkaline medium and that a more rapid reaction had consequently developed. However, when some of these persons died and came to autopsy their lungs showed complicating tuberculosis.<sup>16</sup> A few sections from one of Chapman's patients reviewed by me revealed no evidence of complicating infection, but unfortunately such small blocks of tissue were available that one could not be certain that isolated foci of infection had been overlooked.

14. MacDonald, G.; Piggot, A. P., and Gilder, F. W.: Two Cases of Acute Silicosis (with a Suggested Theory of Causation), *Lancet* 2: 846-848 (Oct. 18) 1930.

15. Chapman, E. M.: Acute Silicosis, *J. A. M. A.* 98: 1439-1441 (April 23) 1932.

16. Kettle, E. H.: Personal communication to the author.

McCord, Fleming, Ainslee and Johnston<sup>17</sup> injected silica with alkalis into the peritoneal cavity of guinea pigs and found that the "primary toxicity" of silica was increased (one out of four of their animals injected with 0.4 Gm. of a mixture of equal parts of either quartz or silica gel and sodium bicarbonate died in four days). There was a wider dispersion of lesions than in the quartz control animals but there was "no proof of either accelerator or inhibitor action of alkalis in the production of silicotic nodules."

The similarity between the lesions found in the various "soap powder cases" and those in sand blasters and in certain tunnel workers<sup>18</sup> suggests the possibility that the rapidity and character of the cellular response might have been produced equally well by excessive concentrations of exceedingly fine particles. Definite proof of acceleration by alkalis is still lacking. It would be more logical to expect an immediate, acute, toxic reaction, the result which McCord and his associates obtained by injection.

**Solubility of Silica.**—Because so much has been written on the solubility of silica as the cause of its irritating properties, mention must be made of the attempts to evaluate this factor. It will be recalled that "the solubility hypothesis" was based on experimental proof of the toxicity of colloidal silica and the fact that quartz is slightly soluble in dilute alkalis. It was postulated that, since the reaction of the mammalian body is slightly alkaline, very fine particles of inhaled quartz might slowly dissolve and form the toxic colloid in the lungs.

Actual demonstration of solution of particulate silica in the living body is difficult both because the amounts are extremely small and because many tissues already contain small but variable quantities of silica which are apparently derived from ingested food. Gravimetric methods of analysis are inadequate to detect minute increases in quantity, and they do not differentiate between undissolved particles and silica in solution. In 1933 King and Stantial<sup>19</sup> modified Isaac's colorimetric method for determining soluble silica for use on biologic material so that it is now possible to detect minute quantities. To ascertain whether such silica is in true molecular solution or in the form of a colloidal suspension, the clear fluid is passed through an ultrafilter to remove the colloidal aggregates. According to King and McGeorge<sup>20</sup> the filtrate theoretically contains only silica in molecular solution.

By this method King, Stantial and Dolan<sup>19</sup> demonstrated an excess of silica in the urine of animals injected with soluble forms of this substance but lesser amounts when relatively insoluble quartz was substituted. They also reported that the urine of silicotic miners contained from four to five times as much silica as that of normal subjects. The latter observation was apparently confirmed by Sayers and Goldman<sup>21</sup> on a group of anthracite coal miners. Goldwater<sup>22</sup> then

showed that the excretion of silica in normal human beings changes from day to day and that even on similar diets the urinary output varies in different workmen. Dworski<sup>23</sup> has confirmed Goldwater's observations and discovered that in addition to the leafy vegetables, which are generally recognized as the major source of ingested silica, certain brands of beer contain surprising amounts of this mineral. Drinking even a half a bottle of such beer will more than double the usual output of silica in the urine. On following the daily excretion in a group of nine tuberculous silicotic miners on ordinary diets for a period of months he found that in six of them the average output in twenty-four hours exceeded the daily average for a control group of normal subjects. However, only two had an average excretion greater than the maximum twenty-four hour output of the controls. In general it would appear that the daily fluctuation in urinary silica of normal persons is greater than the excess in the silicotic over the normal group. At the present time it is not generally conceded that the excretion of silica in the urine is of particular etiology or diagnostic significance.

Theoretically it is debatable whether enough inhaled quartz can be dissolved, produce local tissue reactions and leave a surplus to be excreted in the urine. Comparatively small numbers of particles are inhaled into the pulmonary air spaces at any one time. They are phagocytosed and transported into localized areas where nodular fibrosis then develops. As evidence of local toxic action on the cells there are degenerative changes in the phagocytes and peculiar alterations in collagen. The former closely simulate the "epithelioid" degeneration produced by the tubercle bacillus; the latter consist of swelling, hyalinization and increased absorption of acid dyes. Although it has never been proved, it would seem very likely that most of the soluble silica would be fixed and retained in such reactions. Kraut<sup>24</sup> and later King and his associates<sup>25</sup> demonstrated little or no excess of silica in the blood of persons with silicosis. If it is carried in the blood to the kidneys for excretion it must exist in some other form than the toxic colloid, for anatomic evidence of damage to the kidneys or other organs is lacking. The statistical conclusions of Collis and Yule<sup>26</sup> that all the organs of the body are more frequently diseased in silicotic than in other subjects lack confirmation. To me it still seems probable that if the silica is dissolved most of it combines with the tissues in the immediate vicinity of the particles and that the soluble silica demonstrated in the urine is very largely derived from different foods. A carefully controlled study of the silica balance in hospitalized silicotic and normal subjects is indicated.

Recently many reports have appeared which deal with the solubility of silica outside the body. Some of them can be criticized on technical grounds. For example, Emmons and Wilcox<sup>27</sup> reported the solubilities of fine particles of quartz, flint and various silicates in blood serums. The particles were agitated in the serum at body temperature for periods of several

17. McCord, C. P.; Fleming, R. L.; Ainslee, Harriet, and Johnston, Jan: The Measurement of the Harmfulness of Dusts for Humans Through the Agency of Animal Reactions, Surg., Gynec. & Obst. 63: 129-137 (Aug.) 1936.

18. Gardner, L. U.: The Pathology of So-Called Acute Silicosis, Am. J. Pub. Health 23: 1240-1249 (Dec.) 1933.

19. King, E. J., and Stantial, Helen: The Biochemistry of Silicic Acid: I. Microdetermination of Silica, Biochem. J. 27: 990-1001, 1933.

20. King, E. J., and McGeorge, Murray: The Biochemistry of Silicic Acid: V. The Solution of Silica and Silicate Dusts in Body Fluids, Biochem. J. 32: 417-433 (Feb.) 1938.

21. Goldman, H. F.: Anthracosilicosis Among Hard Coal Miners, U. S. Pub. Health Bull. 221, 1936.

22. Goldwater, L. J.: The Urinary Excretion of Silica in Nonsilicotic Humans: Preliminary Report, J. Indust. Hyg. & Toxicol. 18: 163-166 (March) 1936.

23. Dworski, M.: Unpublished data, Saranac Laboratory.

24. Kraut, Heinrich: Ueber den Kieselsäuregehalt des menschlichen Blutes und seine Veränderung durch Kieselsäurezufuhr, Ztschr. f. physiol. Chem. 194: 81, 1931.

25. King, E. J.; Stantial, Helen, and Dolan, Marjery: The Biochemistry of Silicic Acid: II. The Presence of Silica in Tissues, Biochem. J. 27: 1002-1006, 1933.

26. Collis, E. L., and Yule, G. U.: The Mortality Experience of an Occupational Group Exposed to Silica Dust, Compared with That of the General Population and a Group Exposed to Dust Not Containing Silica, J. Ind. Hyg. & Toxicol. 14: 100-103, 1933.

27. Emmons, R. C., and Wilcox, R. C.: A Study of Silicosis, Am. Mineralogist 18: 100-103, 1933.

weeks; portions of the suspension were then centrifuged at ordinary speeds (up to 3,500 revolutions per minute) to remove the particles, and the supernatant fluids were then analyzed gravimetrically for silica. Since it is doubtful whether all the particles less than 3 microns in diameter were removed from the viscid blood serum by centrifugation and since they determined silica by gravimetric analysis, which would detect both solid and dissolved material, their figures are probably too high.

Titus<sup>28</sup> attempted to overcome these difficulties by separating the particulate silica with an ultrafilter and by analyzing the filtrate colorimetrically, a method which should reveal only dissolved material. But King and McGeorge<sup>29</sup> point out that the dissolved material may exist in both colloidal and molecular solutions. As the colloidal ultrafilters remove not only particulate silica but also colloidal aggregates of dissolved silica, it is their opinion that Titus's very low solubility figures are also erroneous.

In the Saranac Laboratory the amount of soluble silica has been determined colorimetrically on all the physiologic salt solution suspensions of mineral particles used for testing animals. The particles in all cases are of a standard size; all are less than 3 microns in maximum diameter but in many instances those smaller than 1 micron have not been previously removed by elutriation. The suspensions are allowed to stand in a refrigerator until the supernatant fluid is water clear; a portion is decanted and centrifuged at high speed. Although one cannot be positive that every particle has been eliminated by this process, none can be seen; but even if particles were present they would not influence the result of the colorimetric analysis. The figures for free silica in these suspensions vary from values like 5.2 parts per million for active normal quartz to 205 for less active opal. In the case of the silicates the range is equally wide; the slightly irritating clay halloysite yielded 4.5 parts per million, while inert fibrous anthophyllite gave a figure of 124.2. The significance of these results remains to be demonstrated; the obvious deduction is that there is no parallel between the capacity of a siliceous mineral to produce reaction and its degree of solubility in physiologic solution of sodium chloride. Within wide limits the least soluble forms tend to be the most active tissue irritants, but even this is not always the case. For example, normal quartz and diatomite exhibit essentially the same capacity to form fibrosis and yet their corresponding solubility figures are 5.2 and 35 respectively. The moderately irritating opal yielded 205 parts per million of soluble silica, while inert silica gel gave 125 parts of soluble silica. Denny, Robson and Irwin<sup>29</sup> have shown that the solubilities of different samples of pure quartz vary widely, but no one has ever demonstrated a corresponding variation in the rate of capacity to provoke fibrosis. If these test tube experiments parallel conditions in the body, it would seem that some other factor besides solution in water is essential to the production of silicosis.

The last named authors and, shortly thereafter, Briscoe, Matthews, Holt and Sanderson<sup>30</sup> discovered that the addition of other minerals materially affected the

solubility of quartz in water. For example, Denny and his associates reported that the addition of 1 per cent of fine metallic aluminum reduced the solubility of one sample of quartz from 50 to 1.9 parts per million. It was rendered more soluble by adding small quantities of the carbonates and hydroxides of magnesium, sodium, potassium and calcium. Briscoe and his co-workers likewise observed modified solubility of quartz but not always in the same manner and to the same degree; they reported that added magnesium carbonate, alumina and zinc oxide had no apparent effect on the yield of soluble silica from calcined flint, asbestos or feldspar.

These observations *in vitro* are most difficult to evaluate at the present time. The marked influence of other substances on solubility of silica suggests that such experiments may not be directly applicable to the living body. Attempts have been made to overcome the objection by substituting serum or ascitic fluid for water or salt solution as a solvent. King and McGeorge<sup>29</sup> report solubility figures for free and combined silica in these fluids which were comparable to those reported for water. Dworski<sup>23</sup> has obtained similar results in a few tests on normal quartz. King and McGeorge found, however, that the rate of solution was greater with several forms of free silica than with a few of the silicates. But even the use of a body fluid may not approximate conditions in the lungs, where change in hydrogen ion concentration may be more frequent and where the presence of appreciable quantities of other inhaled mineral particles may influence solubility.

Regardless of the mechanisms involved, all the experimental evidence tends to confirm the belief that fibrosis is to be expected only from various forms of free silica and from those silicates which have a fibrous structure; i. e., asbestos. The free silica need not necessarily be of crystalline form; one of the amorphous varieties has proved as active as normal quartz, although others were practically inert. A few of the silicates are toxic; others have produced mild degrees of cellular proliferation. If any of them ultimately cause fibrosis, such reaction must be extremely slow in development. Particles of certain other minerals naturally or artificially associated with free silica delay the development of silicotic fibrosis and modify its form. Whether all nonsiliceous minerals may act as inhibitors awaits demonstration. Definite proof of accelerators to the action of silica is yet lacking; it has been suggested that cases of "rapid silicosis" in human beings may be due to excessive exposures to silica or unusual fineness with or without associated infection.

Some information has been gained on the nature of the irritation produced by different minerals. It may be stated with reasonable certainty that the mechanical factors of hardness and sharpness play no part in the irritation from particulate minerals. With the fibrous silicates mechanical irritation is strongly suspected, although final proof is still lacking. The validity of the solubility hypothesis to explain the unusual activity of free silica has been questioned, and attention has been called to certain apparently well substantiated observations which are not consistent with the hypothesis as now conceived.

#### DUST INHALATION

*Atmospheric Factors.*—As already intimated, there are factors which exert a very marked influence on the behavior of dust suspended in air. If the dust is of

28. Titus, A. B.: Silica and Silicate Solubilities, *J. Indust. Hyg.* 19:138-145 (March) 1937.

29. Denny, J. I.; Robson, W. D., and Irwin, D. A.: Prevention of Silicosis by Metallic Aluminum, *Canad. M. A. J.* 37:1-11 (July) 1937.

30. Briscoe, H. V. A.; Holt, P. F.; Matthews, J. W., and Sanderson, P. M.: Some New Characteristic Properties of Certain Industrial Dusts, *Institute of Mining and Metallurgy, London*, 1937; *Nature, London* 139:753 (May 1) 1937.

uniform composition the factors of specific gravity, particle size, capacity to absorb water and agglutinability largely determine how long it will remain in suspension. Obviously very heavy or very large particles will settle more quickly than smaller and lighter ones; those which remain separated longer than those which clump together and form heavy aggregates. The factor of particle size is of primary importance and has been the one most extensively studied. Sayers<sup>31</sup> has published a graph in which settling velocities are plotted against diameter for particles of various specific gravities. Most particles smaller than 1 micron in diameter settle at a rate of from 1 to 3 feet per hour. When the diameter exceeds 5 microns specific gravity has more influence; for a specific gravity of 7 the rate is 60 feet per hour, for 2.6, the specific gravity of quartz, it is only 25 feet per hour. With the exception of the fibrous materials, it may be said that any particle greater than 10 microns in diameter settles so rapidly that it plays a minor role in the formation of dust.

If the dust is produced from material of complex structure it should not be assumed, as is so often done,

TABLE 5.—Experiments on Inhalation

Type of Rock	Particle Size	Silica Content			Dust from Lungs, 1 to 2 Years' Exposure
		Ground Dust	Rafter Sample	Air-Floted Dust	
Ferruginous chert A	50% > 3 microns Aver. 15 microns 50% < 3 microns Aver. 2 microns	51%	35%	10.5%	3.30%
Ferruginous chert B	93% < 2 microns	67.55	60.0	41.0	16.30
Mixture A Gypsum 1 part Quartz 1 part	All < 3 microns	49.70	53.7	23.3	.....
Mixture B Gypsum 2 parts Quartz 1 part	All < 3 microns	31.40	36.1	17.7	11.20
Quartz control	All < 3 microns	91.24	....	....	43.39

that the proportions of each constituent mineral will be the same either in the air or in the dust settled on the rafters as it was in the original rock. Variations in hardness and brittleness of different components will determine the size to which each will fracture. With a given expenditure of force a hard, tough mineral such as quartz will be broken into larger particles than softer materials. Because of their greater size the quartz particles may largely settle out of suspension, leaving an atmospheric dust composed chiefly of nonsiliceous matter. Numerous experimental and field studies made by the Saranac Laboratory have revealed convincing evidence of such variation in composition. A few examples are cited in the proceedings of the Third Symposium on Silicosis, held in 1937.<sup>31a</sup> Others are to be published in the near future. Hatch and Moke<sup>32</sup> found for example that in foundries the rafter dust might reveal 50 per cent or more of silica but that in air-floated material only 2.3 per cent of the particles under 10 microns in diameter were quartz. Subsequently Moke<sup>32a</sup> retracted his original conclusions because of

errors attributed to his methods of analysis. Even then he was unable to ascertain the exact proportion of free silica in the atmosphere owing to the nature of the other components in the dust. In view of my own experience I am inclined to believe that the original conclusions of Hatch and Moke are still valid. Although many codes are still based on the silica content of the rock to be worked and numerous reports refer to analyses made on samples taken from rafters, it can be appreciated that such figures are not likely to be a reliable index of a dust hazard.

While differences in size, shape and specific gravity may influence the relative settling rates of individual particles in a mixed dust, the factor of agglutination also comes into play and probably has more significance than is the case of dusts composed of only one element. Particles of different physical or chemical structure often agglutinate to form masses so large that they cannot remain in suspension. Opposite electrostatic charges or hygroscopic properties are among the possible causes. If one of the elements happens to be free silica, agglutination with particles of some other mineral may materially reduce the percentage of silica remaining in the atmosphere. Examples of this effect will be cited later when the last group of factors has been discussed.

*Factors of Protective Action of the Upper Respiratory Tract.*—Whether the upper respiratory tract exerts any selective action on different kinds of mineral particles is unknown, but it would seem probable that dusts which are easily wet would be retained more readily than others. From an examination of the mineral particles which have gained access to the lung it is obvious that the protective mechanisms exclude practically all particulate material greater than 10 microns in diameter but that fibrous foreign bodies are not so effectively handled. Fibers of asbestos as long as 150 to 200 microns have been found in the alveoli. It would seem reasonable that aggregates of particles should be excluded in much the same manner as large single particles.

Probably because of the protective action of the upper respiratory tract, the composition of the mineral particles recovered from the lungs is often very different from that of the original rock and sometimes from the dust resulting from its manipulation. Examples from experiments on inhalation are illustrated in table 5.

The total concentrations of atmospheric dust as measured by the impinger method at the breathing level inside the animals' cages were excessive, for the four different experiments cited the average counts of particles less than 10 microns in diameter visible by light field illumination were as follows: chert A, 98,200,000; chert B, 551,800,000; gypsum-quartz mixture A, 319,000,000; gypsum-quartz mixture B, 303,000,000. By dark field illumination these figures were at least four times as high. In each of the chert experiments daily exposures of eight hours continued over a period of two years have failed to produce silicosis in rabbits, guinea pigs and white rats; only nonfibrous patches of chronic pneumonitis resulted. After three years, immature nodular foci of proliferation began to make their appearance.

During similar exposures to both of the artificial mixtures of quartz and gypsum, a few animals which were killed between the twentieth and the twenty-second month have revealed a limited number of atypical hya-

31. Sayers, R. R.: Third Symposium on Silicosis, Saranac Laboratory, 1937, p. 25, Employers Mutuals, Wausau, Wis.  
31a. Durkan, T. M.: Third Symposium on Silicosis, Wausau, Wis., Employers Mutual Liability Insurance Company, 1937, pp. 67-69.  
32. Hatch, Theodore, and Moke, C. B.: Composition of Air-Borne Foundry Dust, *J. Indust. Hyg. & Toxicol.* 18: 91-97 (Feb.) 1936.  
32a. Moke, C. B.: The Solubility of Quartz in Hydrofluosilic Acid, *J. Indust. Hyg. & Toxicol.* 18: 299-300 (May) 1936.



line silicotic nodules in their lungs; those which survived longer had had no nodules but only the non-specific pneumonitis.<sup>33</sup>

The explanation for the retarded development or the absence of silicotic reaction to the inhalation of these mixtures probably involves both the extrinsic and the intrinsic factors that have been discussed. In the case of the ferruginous chert, table 5 indicates that little silica had accumulated in the lung after exposure of one year. What did accumulate would be subject to the modifying action of the iron, previously demonstrated by injection. After three years of exposure enough silica had accumulated to cause reaction, but in the presence of the inhibitor the lesions were still immature and atypical. In the case of the gypsum-quartz mixtures the atmospheric factors were the only ones that have been evaluated. The table indicates low silica values for the lung ash in comparison with the quartz control series. After two and one-half years of exposure appreciable quantities of silica had begun to accumulate, but only in certain animals. Perhaps these were animals in which the protective action of the upper respiratory tract was deficient. The possible effect of intrinsic inhibitory factors has not been tested by injection of gypsum with quartz. In the case of granite dust the results of injection strongly suggest that the inhibition occurs inside the body, but here the extrinsic factors were not tested because facilities for chemical analysis were not available when the inhalation experiments were being made.

Similar inhibitory effects have been reported for metallic aluminum by Denny, Robson and Irwin.<sup>29</sup> These investigators found that the addition of only 1 part of aluminum to 100 parts of freshly fractured quartz prevented the development of silicosis in rabbits. In controls similarly exposed to pure quartz for sixteen hours a day perfectly typical early silicosis developed in six months. Their chemical analyses demonstrated as much silica in the lungs of the experimental animals as in the controls. In this case the inhibition unquestionably occurred inside the body.

Evidences of inhibitory action are not confined to experiments on animals; in industrial plants, reductions in the proportion of inhalable atmospheric silica have been repeatedly demonstrated and delayed responses to silica in mixed dusts are not uncommon. The studies of Hatch and Moke<sup>32</sup> on the reduction of the silica content in the atmosphere of foundries has already been mentioned. Similar observations have been made in unpublished surveys of cement and gypsum plants by Durkan.<sup>34</sup> In the former a quickly setting cement is made by adding a certain quantity of finely ground silica. In an intensive survey of conditions in seventeen such plants a theoretical dust hazard was anticipated from this process, but counts and analyses of the atmospheric dust showed low concentrations of silica at the breathing level. Physical and roentgenographic examinations of the workmen, more than 1,300 in number, have revealed only one person with silicosis attributable to mixtures of silica and cement dust. This man had had a severe crushing injury involving his face and nose which may well have been responsible. A damaged nose could easily impair the effectiveness of the upper respiratory protective

mechanisms. In the gypsum industry, so-called "sanded plaster" was formerly made by mixing considerable quantities of fine and coarse sand with calcined gypsum. Here again the theoretical hazard was found not to exist after a study of the atmosphere and of the employees exposed. By special arrangement with their employers seventeen men, many of them retired, who had had long exposures in making this particular product were located and examined. Both physical and roentgenographic examinations failed to disclose a single case which was even suggestive of silicosis.

But on the other hand it may be objected that silicosis does develop in human beings who are exposed to mixtures of silica and other substances. As a matter of fact there are relatively few industrial atmospheres which are not mixtures, and silicosis does develop in many workmen when the silica content of the dust is sufficiently high. If so many fine silica particles are projected into the air that the other minerals fail to remove them they will be inhaled, but in many cases evidence of inhibitory action will still be manifested by a slow development of pulmonary disease. As examples, the very industries whose dusts have been the subject of experimental study may be cited: granite cutting and hematite mining. If one compares the average exposures that were necessary to produce demonstrable silicosis before the introduction of modern protective methods it will be found that they are much longer in these industries than in ones handling relatively pure silica. In the granite industry exposures of from fifteen to twenty years are commonly necessary to provoke nodular fibrosis; in the hematite mines the average is in excess of twenty years. With the purer silica dust of the lead and zinc mines of Picher, Okla., and the South African gold mines silicosis used to develop in from three to seven years.

In the past it has been customary to explain these variations in the rate of response in different industries on a basis of the relative quantities of free silica in the atmosphere. But the high total concentrations that are known to have existed before the campaign for the prevention of dust began to be effective have made this simple explanation seem inadequate. The action of the two sets of factors just described, one acting outside the body to reduce the amount of silica inhaled and the other inside the lungs to delay and modify the irritating effects of silica, may offer a more satisfactory explanation. Their effects are just beginning to be appreciated, and it will obviously require more study to determine their relative importance in any industrial atmosphere. At the present time it hardly seems justifiable to add protector substances to a siliceous dust as a prophylactic measure; at least, until more is known about the subject, the aim should be to decrease rather than increase the total amount of dust in the atmosphere.

#### FACTORS OF INDIVIDUAL SUSCEPTIBILITY

Up to this point the development of silicosis has been considered from the point of view of the group, and only average periods of exposure have been considered. It is a matter of common knowledge that not all members of any group react to inhaled dust in the same manner nor at the same rate. Every observer has been impressed with the fact that under the former conditions of employment only about one fourth of any group of miners of hard rock would develop silicosis while the other 75 per cent, apparently exposed in the

33. For reasons to be determined, the second gypsum-quartz mixture (2:1) was more active than the first, although the calculated quantities of silica at the breathing zone were almost the same in the two experiments.

34. Durkan, T. M.: Unpublished data from Saranac Laboratory.



same manner, seemed to be immune. Many explanations have been proposed but none are satisfactory. Some have believed that those who escaped were merely persons who did not happen to be exposed to enough dust for a sufficient period of time; some have held that the victims were mouth breathers or persons with deficient upper respiratory protective mechanisms, and still others have entertained the possibility of innate variations in the capacity of tissues to react to silica and other minerals. All investigators are agreed that coexistent pulmonary infection and particularly tuberculous infection plays a profound part in modifying individual susceptibility to inhaled dust.

It is obviously most difficult to prove whether any person in a large plant or even in a particular part of that plant has been subjected to the same quantity and quality of dust as his fellows. What has already been said of the variations discovered in a small experimental chamber 8 by 8 by 8 feet indicates the possibilities in the large spaces of a mine or foundry. Dust counts and analyses may give some idea of average conditions if they are repeated sufficiently often, but no occupational history could possibly account for the rapid local fluctuation and summation of their effects.

Much has been written on effective nasal filtration in preventing or retarding the development of pneumoconiosis. Lehmann<sup>35</sup> has measured the efficiency of the nasal passages in miners and discovered that among men without silicosis 63 per cent had retention efficiencies for inhaled silica dust of over 40, and only 18 per cent fell below 30. In miners with silicosis only 20 per cent of the group had nasal efficiencies over 40, while 62 per cent were classified as less than 30. Lehmann like other observers feels that mouth breathers are in particular danger. These observations seem logical but they have not been confirmed, owing to the difficulty of making the measurements.

There is as yet no proof that the tissues of different normal persons vary in their capacity to react to irritating minerals. With the large doses of free silica employed for the injection tests every animal in any series has exhibited a similar response, and a capacity to react to silica has been proved for various mammals, birds, amphibians and fish. Possibly the injection of much smaller doses would demonstrate individual differences. A most desirable contribution would be a large series of chemical analyses of the lungs of both silicotic and nonsilicotic members of a human group exposed to some siliceous dust for a significant period of years. Intensive biochemical studies of both groups are also needed to answer this question.

The factor of infection is the cause for variation in susceptibility which has been studied most intensively. Relatively little is known of the effect of infections in the upper respiratory tract, although it is assumed that such conditions modify the protective mechanisms.

In the case of the lungs themselves there is no doubt of the etiologic significance of chronic infections. This complication may produce anatomic alterations which mechanically influence the deposition of inhaled dust, and it may possibly act in more subtle ways to alter the tissue responses to certain kinds of dust.

The mechanical effects are familiar and most easily understood. In normal lungs inhaled particles are probably distributed quite uniformly throughout the

organs, except for a tendency to accumulation in the subpleural air spaces. By the agency of mobile phagocytes, ordinary quantities of such particles are removed from the air spaces and transported to the lymphatic vessels. Through the latter the foreign bodies are carried to lymphoid tissues situated both within and at the roots of the lungs. The development of a focus of chronic infection interferes with this orderly process of deposition and elimination. Appreciable numbers of air spaces may be obliterated by granulation or scar tissue, and the lymphatic drainage from the affected area is disturbed or perhaps destroyed. Particles of dust accumulate in increasing numbers about and within such an area of disease. The pigmented scars of healed tuberculosis in the apexes of the lungs are familiar examples of this tendency. The infectious process may be more extensive and may possibly have exhibited a considerable degree of pathologic activity during periods of inhalation of dust, but the same tendency to local accumulation is manifested. The subsequent development of emphysema and other changes to be discussed in the section on pathology may then make it appear that all the dust has localized in the region of the infection.

The more subtle influences of infection and particularly tuberculous infection in apparently altering the capacity of the lungs to react to siliceous dusts are not well understood. There are some investigators who believe that mature silicotic lesions never develop except in the presence of an element of infection. I do not subscribe to this view as I believe that the injection and inhalation experiments with pure silica have reproduced nodular fibrosis under conditions in which infection can be excluded. Nevertheless I admit that in some human lungs with even a localized focus of healed tuberculosis the nodules of silicotic fibrosis throughout all parts of the organs are of unusual size and appearance. I<sup>36</sup> have repeatedly maintained that the tubercle bacillus and silica dust in combination can produce results which neither irritant alone will do. With mixtures of free silica and other substances the inhibitors have not had their usual effects in animals infected with tubercle bacilli. The silicotic lesions have progressed more rapidly, and, while the tuberculous element has either healed or become very chronic, much more fibrosis has developed than with either infection or the dust alone. I have entertained the hypothesis that at least some of the silicates may prove to be more active on a background of infection than in normal lungs. Uncompleted experimental observations lend some support to this view, but the only silicate with which conclusive results have thus far been attained is chrysotile asbestos. Inhalation of this dust in association with any pulmonary infection has caused healing with much more fibrosis than either infection or asbestos alone. All these points will be more fully discussed in the section on pathology. Here it suffices to state that chronic infectious lesions and particularly those due to tuberculosis alter the localization and accumulation of all dusts in the lungs, that under proper circumstances they accentuate the development of silicotic fibrosis and that they permit both mixtures of free silica with other dusts and the silicate asbestos to produce unusual amounts of scar tissue.

7 Church Street.

35. Lehmann, Gunther: Dust Filtering Efficiency of the Human Nose and Its Significance in the Causation of Silicosis, *J. Indust. Hyg.* 17: 37-40 (March) 1935.

36. Gardner, L. U.: The Relatively Early Lesions in Experimental Pneumoconiosis Produced by Granite Inhalation and Their Influence on Pulmonary Tuberculosis, *Am. Rev. Tuberc.* 4:734-755 (Dec.) 1920.

## Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION  
OF THE FOLLOWING REPORTS. HOWARD A. CARTER, Secretary.

### NU-HESIVE SURGICAL DRESSINGS ACCEPTABLE

Manufacturer: Diadem Surgicals, Inc., Leominster, Mass.

New products utilizing Nu-Hesive Gauze Bandage as a base (acceptance published in *THE JOURNAL*, March 30, 1935, p. 1073) are recommended for use as sterile bandage or dressing material. Nu-Hesive is a nonabsorbent, porous material that traps excretions, adheres only to itself, and does not shrink when wet. Gauze is impregnated with a practically nonabsorbent cohesive latex which leaves the interstices of the fabric partially open. In addition to the Nu-Hesive Gauze Bandage previously accepted, the line includes Bias Bandage, Dia-Dressings, Finger Wraps, Gauze Tape Bandage and Ortho-Hesive Athletic Tape.

**Nu-Hesive Bias Bandage:** A bias bandage having considerable elasticity and binding pressure, in a range of sizes, used where excessive swelling is imminent or a slight flexing of the joint is desired.

**Nu-Hesive Dia-Dressings:** A prepared sterile compress, recommended in wet applications and as a dressing for boils, and ulcers. It is wrapped in individual glassine envelopes.

**Nu-Hesive Finger Wraps:** A prepared, sterile finger dressing, for minor injuries, wrapped in glassine envelopes.

**Nu-Hesive Gauze Tape Bandage:** A combination, nonshrinking tape and gauze bandage, packed in sterile rolls, especially useful in wet dressings.

**Nu-Hesive Ortho-Hesive Athletic Tape:** Primarily designed for ankle strapping for athletes; also useful in ankle and wrist support in serious sprain cases. Normal muscle flexing is permitted by a primary give or spring, and support becomes effective immediately following the limit of normal muscle action. The Ortho-Hesive Athletic Tape is not subjected to the same sterilization process since it is not intended to be used in contact with open wounds.

The firm was asked to substantiate the claims made for sterility and in reply submitted laboratory records, photographs of the testing laboratory in the finishing and packing rooms, and a test rack containing samples which had each been incubated for at least ninety-six hours at 37 C.

In addition, the materials were subjected to a bacteriologic examination by a competent medical man, at the Council's instigation. The report is abstracted here:

**Materials and Methods.**—Culture medium consisted of nutrient broth in large tubes (50 cc. in each tube) which was sterilized by 15 pounds steam pressure for twenty-five minutes. Instruments used in handling the gauze were wrapped in paper and sterilized by exposure to a temperature of 160-170 C. for at least two hours. All manipulations were carried out in a glass-walled box with an opening in the bottom on one side for the operator's arm. This opening was swabbed out thoroughly with saponated solution of cresol and kept closed for several hours before use.

The rolls of gauze were carefully unwrapped at one end and then securely grasped with a pair of heavy forceps by inserting one jaw through the hole in the center of the roll and the other jaw through the inner turns of the gauze. The wrapper was then entirely removed without allowing the outside of the wrapper to touch the gauze. By means of a safety razor blade held in a hemostat a number of deep cuts 0.5 cm. apart were made across the roll of gauze parallel to its axis. By means of a pair of forceps these sections were lifted out and placed immediately in the culture tubes. The inner spool, together with the few remaining turns of the gauze, was also cultured so that the entire roll of gauze was cultured each time.

The Finger Wraps and Dia-Dressings were opened by cutting off the end of the containing envelop. With sterile forceps the gauze was removed, rolled into a small roll and the entire piece placed in a culture tube. The tubes were incubated at 37 C.; half of the tubes of each series were incubated aerobically, the other half anaerobically in a sealed jar. It was shown that *Clostridium sporogenes* grew readily in broth tubes in the jar.

With each series of gauze culturing a number of broth tubes were opened and closed in the same manner as those receiving the gauze. These were incubated both aerobically and anaerobically.

**Summary of Results.**—One hundred and sixteen pieces of gauze, representing all the products submitted, were cultured in nutrient broth aerobically and anaerobically. No bacteria grew in any of the tubes. On inoculation of these tubes with *Staphylococcus aureus* and *Bacillus subtilis* growth occurred readily, with the exception of four series.

These were numbers 2, 9, 19 and 20, consisting of one-half inch Gauze Tape Bandage, 1½ inch Gauze Tape Bandage, 3 inch Bias Bandage and 4 Dia-Dressings (2 inches by 4 inches) respectively. Only slight growth in these showed that there is one inhibitory substance that is present in some of the preparations of gauze. This inhibition could not be correlated with any type of gauze or time of incubation. Since the inhibition was present in only a few of the rolls and then not in sufficient degree to prevent bacterial growth entirely, no attempt was made to remove the inhibitory substance. The tubes not showing this inhibition on inoculation showed as much growth as the control tubes.

It may be said that no bacteria were cultured from the products submitted, under conditions in which growth of ordinary bacteria occurred readily.

In view of the foregoing report, the Council on Physical Therapy voted to reaccept the Nu-Hesive Gauze Bandage and accept the Bias Bandage, Dia-Dressings, Finger Wraps, Gauze Tape Bandage and Ortho-Hesive Athletic Tape.

### EMERSON HUMIDOX HUMIDIFIER ACCEPTABLE

Manufacturer: J. H. Emerson, 22 Cottage Park Avenue, Cambridge, Mass.

The Emerson Humidox is a humidifier for use in connection with an oxygen regulator and nasal catheter for administering oxygen to patients. It consists of a quart preserve jar with a metal cover equipped with an inlet which is attached to the regulator and an outlet which leads to the catheter. The inlet pipe goes to the bottom of the jar, which is partially filled with water. At the lower end of this pipe is a porous filter which breaks up the oxygen into very fine bubbles, allowing it to take up slightly more moisture than would be possible with an ordinary wash bottle, according to the firm.

The apparatus may be purchased with a carrying case and additional equipment including a regulator, catheter and wrench. When the Aircor float type gage is used, corrections have to be made for the indicated flow. These are mentioned in the direction sheets.

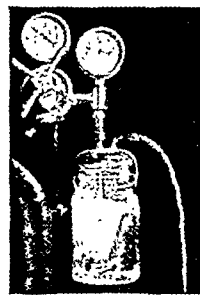
With the large cover of the preserve jar held in place by a resilient fastener, any excess pressure causes this to act as a safety valve. Water does not pass through the walls of the porous filter rapidly, which aids in preventing sudden high pressures from escaping from the regulator into the jar and hence to the patient. In addition, it acts as a protection in case the humidifying jar is tipped over.

A separate heater may be hung on the humidifier. This raises the temperature of the water from 10 to 15 degrees, depending on the size of heating element used (from 10 to 30 watts). It is claimed that the warmed oxygen is better for the patient.

The only therapeutic claim made for the device by the manufacturer is that it will reduce the danger of drying out the nasal passages and the oropharyngeal mucosa when oxygen is being administered by nasal catheter.

In order to substantiate claims made for the unit, it was investigated clinically by a competent physician. He reported that it rendered satisfactory service.

In view of the foregoing report, the Council on Physical Therapy voted to accept the Emerson Humidox Humidifier for inclusion in its list of accepted devices.



Emerson Humidox.

# THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, NOVEMBER 19, 1938

## ANIMAL EXPERIMENTATION AND SCIENTIFIC MEDICINE ENDORSED BY VOTERS

The voters of California and Colorado, November 8, by overwhelming majorities emphatically rejected proposals made in those states to undermine the structure of scientific medicine. In California an initiative humane pound law, so called, proposing to cripple scientific research by hampering animal experimentation, was decisively defeated. In Colorado an initiative measure proposed by a group of chiropractors, to debase the quality of medical care in the state by repealing the basic science act and by destroying other safeguards that have been erected to assure adequate and scientific medical service, was met by an avalanche of negative votes, running as high as ten to one in some counties.

In Oklahoma an initiative measure that would have sanctioned practices not conducive to public welfare failed to get on the ballot, because of court action instituted by the medical profession. In Ohio a chiropractic initiative somewhat similar to the Colorado initiative died aborning, the cultist sponsors apparently becoming disheartened shortly after the proposal was submitted to the attorney general for his approval as to form. Petitions in Ohio were not circulated and the proposed initiative measure was not submitted to the people for a vote.

The medical associations in the states named assumed the lead in thwarting the selfish interests behind these proposals, interests that would subordinate the public welfare to their own private ends. In California and Colorado the state medical associations, aided by many lay and other professional groups and by public spirited citizens, informed the people fully of the dangers implicit in the proposals. To bring these dangers to the attention of the voters necessitated great sacrifices of time and money, but the results show that such sacrifices were well worth while and indicate that an informed electorate will support scientific medical care under proper legal and ethical safeguards.

## INJURIES TO THE RECURRENT LARYNGEAL NERVE

The recurrent laryngeal nerve is a branch of the vagus nerve which on the right side arises in front of the subclavian artery and on the left side to the left of the arch of the aorta. On each side the nerve ascends in the groove between the trachea and the esophagus and enters the larynx, branches going to all the muscles except the cricothyroideus. An injury to both recurrent nerves in the course of a thyroid operation is a calamity.

The prevailing attitude of surgeons toward the recurrent nerves, which is partly erroneous, has been unchanged from the beginning of thyroid surgery. Kocher's position in advocating that partial thyroidectomy be done under local anesthesia so that, in having the patient speak, the surgeon might learn that the recurrent nerves were not injured, was unsound. There are temporary changes in the voice in some patients immediately after and probably during thyroid operations without injury to the recurrent nerves, and, if the voice change does indicate an injury to the nerve, the damage has already been done. Other unsubstantiated impressions about the recurrent nerves have been accepted for many years. Surgeons have assumed that the nerves were too small to dissect and that, when possible, dissection would result in recurrent nerve paralysis. It has also been assumed that direct suture of severed recurrent nerves was impossible because the nerves could not be found in the scar tissue following subtotal thyroidectomy and if found they would be too small to suture. Recent experience at the Lahey Clinic<sup>1</sup> has shown that these assumptions are false. Three years ago Lahey undertook to demonstrate the recurrent nerve in practically all thyroid operations. To date the surgeons of that clinic have dissected more than 3,000 recurrent nerves, thus showing not only that the nerve is sufficiently large to be dissected but that it can be palpated as it is pushed laterally against the tracheal wall; also that routine dissection and even palpation while on a moderate stretch cause no interference with function. Moreover, this experience has proved that the routine exposure of recurrent nerves in thyroid surgery will diminish, if not largely eliminate, injuries to that nerve.

There is still some confusion about the clinical features of recurrent laryngeal nerve paralyses. If the recurrent nerves are interrupted there is usually little difficulty with the patient's breathing during the operation, but immediately after the operation the patient is unable to talk because of loss of innervation of the vocal cords. Frequently within six months the patient may report that the voice is returning. Somewhat later the patient will complain of inability to breathe satisfactorily after any unusual activity, and this condition will progress until there is difficulty with breathing on

1. Lahey, Frank H., and Hoover, Walter B.: Injuries to the Recurrent Laryngeal Nerve in Thyroid Operations; Their Management and Avoidance, *Ann. Surg.* 108: 545 (Oct.) 1938.

slight exertion. Permanent bilateral abductor paralysis causes obstruction of the larynx by the mesial position of the vocal cords, relief from which often necessitates the permanent use of a tracheotomy tube.

After demonstrating the ease with which severed recurrent nerves can be approximated, Lahey states that, in all cases in which there is such an injury which does not disappear in three months, the nerve should be explored and the ends refreshed and anastomosed. The previous attitude generally has been that in such injuries nothing much could be done. In a case in which both nerves had been severed elsewhere ten months previously they were found and anastomosed without difficulty. One great difficulty of suturing recurrent nerves is that of approximating abductor fibers with abductor fibers and adductor fibers with adductor fibers. At present it is impossible to say whether restoration of double impulse nerve conduction in a single trunk can ever be successfully accomplished. One should, however, in anastomosing recurrent nerves make every effort to unite them so that there may be at least a reasonable chance of fibers conveying similar impulses being opposed to each other. With magnifying lenses it can be seen that the nerve is somewhat flattened. In uniting it the surgeon should place the two ends of the nerve in the same flat plane and with no twist in them. When more than half an inch to an inch is lost it is doubtful whether the severed ends of the nerve will come together.

Even though thyroid surgery is now well established on a sound basis, there is still need for more interest among surgeons in diminishing the incidence of injury to recurrent laryngeal nerves.

#### MIXED TUMORS OF THE LUNG

Discrepancies between the microscopic diagnosis and the clinical behavior of tumors are not infrequent. Cole<sup>1</sup> has recently cited many examples of gastric ulcer in which the estimation of malignancy varied decisively among various diagnosticians. A newer and more difficult problem concerns the diagnosis of tumors of the bronchi.

Formerly tumors of the lung were considered rare and quite unsusceptible of surgical attack, even when benign. Now, however, the point of view has changed. Not only are benign tumors considered suitable for successful surgical excision but even malignant neoplasms have been shown to be removable with comparative safety and with a reasonable chance of cure. With the emphasis on early diagnosis has come the identification of the early clinical manifestation of these tumors. The symptoms produced by pulmonary tumors are now becoming more generally known. With the advent of bronchoscopy their early stages are actually seen and biopsy specimens obtained and studied. Whereas our

knowledge of neoplasms of the lung was formerly based on necropsy material, now bronchoscopic examinations with study of biopsy specimens are more frequent. With this advance has come an apparent increase in the incidence of such lesions but with it a confusion as to their actual nature. Especially important is the estimation of the malignancy of these early tumors. On such a diagnosis must rest the decision as to the most appropriate type of therapy. Many of them have been called adenomas, others have been described as polyps, a few as chondromas, fibromas, angiomas and neurofibromas.

When a patient complains of chronic cough, hemoptysis, pain in the chest or unexplained fever, the diagnosis of influenza or unresolved pneumonia may seem logical and correct. In many instances, however, a small tumor will be found occluding a bronchus, producing atelectasis or associated with pulmonary suppuration. With bronchoscopic relief of the obstruction the symptoms may disappear. However, microscopic study of the excised tissue may reveal a benign or a malignant lesion. Shall it be treated with diathermy, roentgen therapy or radium, or does surgical excision offer the only secure hope of cure? The answer to these questions is the subject of an anatomic and clinical study of many of these cases, recently reported in the *Ludvig Hektoen festschrift* by Womack and Graham.<sup>2</sup> These observers present evidence to show that many pulmonary neoplasms resemble fetal pulmonary tissue and arise from the failure of embryonic buds to develop into normal structures. Recognizing their similarity of behavior and in some respects their similarity of origin to the mixed tumors of the parotid gland, these workers have described this group of neoplasms as mixed tumors of the lung and have built up a histologic and clinical entity to fit their observations.

This new concept of pulmonary neoplasms will probably go far to explain the discrepancies which have been experienced in the microscopic appearance and clinical behavior of many tumors of the lung. As Womack and Graham point out, these tumors arise from entoderm and mesoderm and hence may take various forms depending on the tissue they resemble. More important is the fact that these tumors, though at first benign, may eventually develop into carcinoma and are to be considered, therefore, as potentially malignant. By the time they do become malignant their pathogenesis is lost and they may look like the ordinary type of bronchiogenic carcinoma. Thus is explained the failure of postmortem studies to recognize this group of tumors. With the realization of their common origin as mixed tumors, Womack and Graham feel on the basis of their studies that such terms as adenocarcinoma, alveolar carcinoma, mucous gland carcinoma, "oat cell" carcinoma and round cell carcinoma are now untenable. With this simplification in the terminology as well as

1. Cole, L. G.: *The Pathological Yardstick: Its Accuracy as an Instrument for Measuring Errors in Clinical, Roentgenological and Surgical Diagnosis of Gastric Lesions*, Surg., Gynec. & Obst. **63**: 689 (Dec.) 1936.

2. Womack, N. A., and Graham, E. A.: *Mixed Tumors of the Lung: So-called Bronchial or Pulmonary Adenoma*, Arch. Path. **26**: 165 (July) 1938.

pathogenesis, the study of the early manifestations of pulmonary neoplasms will be facilitated. Perhaps the growing incidence of the late stage of inoperable cancer of the lung may be halted by a recognition of the lesion which in many cases seems to be its precursor.

## Current Comment

### BUILD OF WOMEN AND MORTALITY

In a preliminary report read before the Association of Life Insurance Medical Directors of America, Dublin and Marks<sup>1</sup> discussed the results of their investigations on the relation of height and weight of women to the death rate. Their descriptive tables are based on 329,627 policies and their mortality tables on 308,228 policies—material extensive enough for statistical conclusions in most classes even though derived from the experience of a single company. When all heights were combined, the most favorable mortality in ages under 30 was found among those slightly (from 5 to 14 per cent) and moderately (from 15 to 24 per cent) overweight; but the ratios for these groups were not significantly different from those of average weight. From these low levels the mortality increased to its highest point in the 25 to 35 per cent overweight, followed closely by those from 15 to 24 per cent underweight. At ages 30 to 39 the situation was in many respects similar. At ages 40 to 49 the best mortality was recorded among those slightly below average weight, and at ages 50 and over the most advantageous mortality was among those who were underweight. In the aggregate the mortality of women of short height has been distinctly above the average, and the ratio of actual to expected deaths was 109 per cent for this group as compared with 98.8 per cent recorded for both medium height and tall women. This excess mortality of short height women appeared in every age group. At ages under 30 the most favorable mortality was recorded among medium height women, but between 30 and 39 tall women have done best. In women over 40 there was in the aggregate no marked difference between the mortality ratio and the medium height and tall women. When related to specific diseases, mortality from tuberculosis was 60 per cent higher among those 15 per cent or more underweight than the average for the group. In those 15 per cent or more overweight the mortality was only 33 per cent of the expected. The mortality from pneumonia and influenza followed a similar pattern. Deaths from lobar pneumonia were highest among the underweight and those considerably overweight, although this trend showed much variation with age. For the chronic cardiovascular and renal conditions there was a fairly steady progression of the ratios from the lowest levels in the underweight groups to the highest in the overweight groups. Acute heart and kidney disease, on the other hand, tended toward high frequency among the underweight. Diabetes showed the typical correlation between weight and mortality far more distinctly than did most

other causes. The most striking differences in mortality were found in diseases of the gallbladder and biliary passages, where there was an unmistakable progression of mortality from a low point among the underweight to a high point among those who were more extremely overweight. This study, while of a preliminary nature, apparently serves to confirm the general assumption that has been made in the insurance business with regard to the build of women; namely, that they present a situation similar to that disclosed by the studies of the influence of build on mortality among men. Furthermore, these authors believe, the anthropometric data indicate the need of some revision of the standard height-weight table, which is too smooth and therefore probably disregards fundamental changes in weight according to age during adult life. It is their opinion that median weights are probably better than mean weights because the latter are unduly influenced by extreme overweight.

### TRANSPLANTATION OF HUMAN CANCER INTO RABBITS

Recently successful transplantation of human cancer into the anterior chamber of the rabbit eye has been reported. This is potentially an exceedingly important contribution to experimental pathologic technic. About a year ago Greene and Saxon<sup>2</sup> of the Rockefeller Institute, Princeton, N. J., tested the autoplasmic and homoplastic transplantability of rabbit uterine adenomas and adenocarcinomas. While autotransplantations were invariably successful, intratesticular, subcutaneous, intramuscular and intraperitoneal transplantations into a new host invariably failed. Transplantations into the anterior chamber of the eye of a new host, however, were successful in a large percentage of the cases. After growth for from three to five serial transplants in the anterior chamber of the eye, successful transplants could be made into the testicle. With this encouraging result, the Rockefeller Institute experimenters retested the possibility of heteroplastic transplantation. Heteroplastic transfer of mammalian tissues is generally considered impossible. Two tumors, an adenocarcinoma of the rabbit uterus and an adenocarcinoma of the rabbit breast, however, were successfully transplanted into the guinea pig eye. Serial transplants through three generations were effected, a process which apparently could be continued indefinitely. In his latest report Greene<sup>2</sup> tells of attempts at similar heteroplastic transplantation of a human breast tumor. Seven successful takes were obtained in twelve attempted transplantations into the anterior chamber of the rabbit eye. Growth first became apparent toward the end of the third week, with vascularization readily visible during the sixth week. Following vascularization the growth rate increased. Since the behavior of the human cancer grafts in the rabbit eye conforms in all respects to those of rabbit tumors in the guinea pig eye, Greene believes that human tissues can thus be maintained and cultivated indefinitely in the rabbit. If so, his technic may be applicable to a wide range of physiologic and pathologic problems not associated with malignant growths.

1. Dublin, L. I., and Marks, H. H.: The Build of Women and Its Relation to Their Mortality, read at the forty-eighth annual meeting of Association of Life Insurance Medical Directors of America, Oct. 29, 1937.

1. Greene, H. S. N., and Saxon, J. A., Jr.: *J. Exper. Med.* 67: 691 (May) 1938.

2. Greene, H. S. N.: *Science* 88: 357 (Oct. 14) 1938.

# ORGANIZATION SECTION

## HOUSE OF DELEGATES COMMITTEE MEETS WITH INTERDEPARTMENTAL COMMITTEE

On October 30 the Committee of the House of Delegates of the American Medical Association, including Dr. Irvin Abell, President of the Association, as chairman; Dr. Walter F. Donaldson, Pittsburgh; Dr. Walter E. Vest, Huntington, W. Va.; Dr. Henry A. Luce, Detroit; Dr. Fred W. Rankin, Lexington, Ky.; Dr. Frederic E. Sondern, New York; Dr. E. H. Cary of Dallas, Texas, with Dr. Rock Sleyster, President-Elect of the American Medical Association, and Dr. Olin West, Secretary, ex officio, met with the Interdepartmental Committee to Coordinate Health and Welfare Activities of the Government in Washington. The Interdepartmental Committee arranged for attendance by several members of its own Technical Committee, and the American Medical Association group was accompanied by Dr. W. C. Woodward of the Bureau of Legal Medicine and Medical Legislation and Dr. R. G. Leland and Mr. Jack D. Laux of the Bureau of Medical Economics.

In a joint interview, following the conference, by Dr. Irvin Abell and Miss Josephine Roche, it was pointed out that the conference had reached no definite conclusions or specific plans for cooperation, nor had there been any abandonment of specific positions taken by either group in relationship to the program. The representatives of the government again explained the detailed concept of the National Health Program. The representatives of the American Medical Association indicated the actions taken by the House of Delegates, which involved approval of the extension of public health service specifically related to the prevention of disease and the provision of hospitals and allied

institutions and of government assistance for the care of the indigent when the need can be established. The medical representatives pointed out that in hospitalization and the care of the indigent the administration should be simple and placed in the hands of responsible public officials who would cooperate with local medical societies. The medical representatives again expressed opposition to compulsory sickness insurance and the fear of the fact that the insistence on such a system by the government would be "bureaucratic, costly and political."

In a brief report on the conference, President Irvin Abell said:

The reception accorded our committee was quite friendly and the discussions evinced the same spirit on both sides. They were fruitful in bringing out a better understanding of opposing points of view and in focusing attention on the discrepancies in data and statistics on which such points of view are founded. While tentative agreement in principle, not in methods of application, was reached on four of the recommendations, the conference was stymied by the question of compulsory sickness insurance. The Interdepartmental Committee is to hold conferences with representatives of other groups, notably the American Public Health Association, the American Dental Association, the American Hospital Association and the American Nursing Association. It was suggested that our committee return at a later date for further conference presumably after the above named organizations, through their representatives, have had opportunity to express their views. If this invitation is accepted an early date was suggested, as the Interdepartmental Committee will prepare its report to be submitted to the President at the opening of the Congress, when its recommendations may be embodied in proposed legislation.

## ABSTRACT OF REPORT OF SPECIAL COMMITTEE OF THE AMERICAN DENTAL ASSOCIATION

Your committee [of the House of Delegates of the American Dental Association] has drawn up the following declaration of principles and recommendations which it believes should be presented by the American Dental Association to the federal government for its assistance in planning the dental phase of a general health program.

Your committee recommends that in the formulation of any national health program the American Dental Association should insist on including the following principles:

I. In all conferences that may lead to the formation of a plan relative to a national health program, there must be participation by authorized representatives of the American Dental Association.

II. The plan should give careful consideration to: first, the needs of the people; second, the obligation to the taxpayers; third, the service to be rendered; and, fourth, the interests of the profession.

III. The plan should be flexible so as to be adaptable to local conditions.

IV. There must be complete exclusion of nonprofessional, profit-seeking agencies.

V. The dental phase of a national health program should be approached on a basis of prevention of dental diseases.

VI. The plan should provide for an extensive program of dental health education for the control of dental diseases.

VII. The plan should include provision for rendering the highest quality of dental service to those of the population whose economic status, in the opinion of their local authorities, will not permit them to provide such service for themselves, to the extent of antepartum care, the detection and correction of dental defects in children, and such other service as is necessary to health and the rehabilitation of both children and adults.

VIII. For the protection of the public, the plan shall provide that the dental profession shall assume responsibility for determining the quality and method of any service to be rendered.

### RECOMMENDATIONS

Your committee has considered the five recommendations of the Technical Committee and, so far as they apply to dental service, makes recommendations as follows:

*Expansion of Public Health and Maternal and Child Health Services.*—Expansion of General Public Health Services: 1. We approve of the general expansion of public health services and, in addition, recommend the establishment of a federal Department of Health with a secretary who shall be a graduate in medicine, and a member of the President's cabinet; and a first assistant secretary who shall be a graduate in dentistry.



2. In an expanded public health program which involves a consideration of the expenditure of millions of dollars for public health purposes, your committee recommends that the problem of dental caries and other dental diseases be included.

*Medical Care for the Medically Needy and a General Program of Medical Care.*—1. Your committee is convinced that satisfactory dental service cannot be rendered under a compulsory health insurance system. We therefore do not favor such a plan but do approve voluntary budget plans under professional control which will enable patients to "apportion costs and timing of payments so as to reduce the burdens of [dental] costs and remove the economic barriers which now militate against the receipt of adequate [dental] care."<sup>1</sup> [The word "dental" was substituted by the committee for the word "medical" in the original quotation.]

2. The committee approves the recommendation that such a program should provide for "continuing and increased incentives to the development and maintenance of high standards of professional preparation and professional service."<sup>1</sup>

#### CONCLUSION

Your committee agrees with the Technical Committee's belief "that, as progress is made toward the control of various diseases and conditions, as facilities and services commensurate with the high standards of American medical practice are made more generally

available, the coming decade, under a national health program, will see a major reduction in needless loss of life and suffering—an increasing prospect of longer years of productive, self-supporting life in our population."<sup>2</sup> We also believe that the above statements apply equally to dental practice and that the enumerated benefits would be enhanced by early and regular dental care in childhood.

Your committee offers two final recommendations:

1. In view of the fact that dental caries is the most prevalent disease of mankind, the American Dental Association strongly recommends that the federal government augment, with a comprehensive research program, the efforts of the organized dental profession to determine the cause of this disease.

2. That in keeping with the first main principle of this report, a committee of five practicing dentists be appointed by the Board of Trustees, together with such technical advisers as the needs of the committee require, to fulfil the provisions of principle I.

#### COMMITTEE

HOMER ROBISON.	W. O. TALBOT.
CRAFT A. HOPPER.	ALFRED WALKER.
E. E. VOYLES.	STANLEY RICE.
HENRY CLINE FIXOTT.	R. J. RINEHART.
HAROLD W. OPPICE, Chairman.	

1. "A National Health Program," recommendation 4, paragraph 4.

2. "A National Health Program," recommendation 5, last paragraph.

## OFFICIAL NOTES

### HEARINGS BEFORE THE GRAND JURY IN WASHINGTON

In addition to witnesses mentioned in recent issues of THE JOURNAL, the newspapers report the following persons as having appeared last week before the Special Grand Jury in Washington, D. C.: Dr. Lewis H. Taylor, president of the Sibley Hospital; Mr. and Mrs. Charles Hardin; Mr. Sherwood Booth; Miss Tommie Lee Nix and Miss Elizabeth Tew, employees of the Home Owners' Loan Corporation; Miss Taylor Owen (the last three were said to be members of the Group Hospital Association, Inc.); Mrs. Peggy O'Connor and Mr. James R. Adams, both employees of the WPA; Miss Sarah Abbott, Mrs. Harriet A. Austin, Mr. and Mrs. H. P. Avery, all said to be members of the Group Health Association, Inc., and Dr. William W. Bauer, director, Bureau of Health Education, American Medical Association. The Grand Jury is also said to have had before it during the last week records of Garfield Memorial Hospital, brought by Dr. Francis J. Eisenman, superintendent, and records of Columbia Hospital for Women and Lying-In Asylum, brought by Col. P. M. Ashburn, superintendent of that hospital.

### RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the

National Broadcasting Company, entitled "Your Health," began Wednesday October 19 and will run consecutively for thirty-six weeks. The program is broadcast over the Blue network of the National Broadcasting Company each Wednesday at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).<sup>1</sup>

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The next six programs to be broadcast, together with their dates and their topics, are as follows:

November 23.	Weather and Wearing Apparel.
November 30.	Rest, Relaxation and Recreation.
December 7.	Tuberculosis and the Teens.
December 14.	What Shall We Eat?
December 21.	Hidden Treasures in Foods.
December 28.	Good Milk, Good for You.

1. Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over Station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.

## WOMAN'S AUXILIARY

### California

The Santa Barbara County auxiliary recently gave \$34 to the troupe of Girl Scouts it sponsors in order that two girls might attend camp two weeks each.—At a benefit dinner at the residence of Dr. and Mrs. William Daniel, Pasadena, \$370.66 was realized with which a resuscitator for babies was purchased and presented to St. Luke's Hospital, Pasadena.—The Santa Clara County auxiliary is holding a series of 50 cent teas in private homes, the profit from which is turned over to the

charitable fund, with which a number of children each year are sent to camps.

### Washington

Mrs. J. B. Robertson of the auxiliary to Pierce County Medical Society, Tacoma, won the special cash prize of \$25 offered by the "Hygeia" Committee of the Woman's Auxiliary to the American Medical Association for the best paper on "The Value of 'Hygeia' to the Medical Profession." Only the auxiliaries winning cash prizes or honorable mention in the second Hygeia annual contest were eligible to participate.



## Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

### CALIFORNIA

**Proposed "Humane Pound" Law Defeated.**—The so-called humane pound initiative measure was defeated in the California election November 8 by a margin of more than two to one, according to press reports. Up to November 10 the totals were 1,259,014 votes against the measure and 593,934 in its favor.

**Changes in Health Officers.**—Dr. Alexander B. Bigler has been appointed city health officer of Chowchilla, succeeding Dr. Alton C. Atwood. Dr. Cornwall C. Everman is health officer of Larkspur and Dr. David G. Smith of Corte Madera; both of these communities were formerly served by Dr. Louis L. Robinson. The city of Needles has transferred the administration of its public health affairs to the San Bernardino County full time health unit; Dr. Walter W. Fenton is the health officer of the county. Dr. Frederick W. Knight has been appointed health officer of Corcoran to succeed the late Dr. James H. Van Vorhis.

### CONNECTICUT

**Society News.**—Dr. Morton Arnold, Willimantic, addressed the Tolland County Medical Association October 18 in Somers on "Treatment of Common Diseases of the Ear, Nose and Throat."—The Hartford County Medical Society was addressed October 25 in Bristol by Dr. Abraham Myerson, Boston, on "Relationship of the Autonomic Nervous System to Pharmacology."—Dr. John A. Hartwell, New York, discussed "Trends in Medical Practice" before the New Haven County Medical Association October 27.—Dr. Rudolf Schoenheimer, New York, discussed "Studies in Protein Metabolism with the Aid of Heavy Nitrogen" before the Yale Medical Society November 9 in New Haven.

**Changes in Health Officers.**—Dr. Robert E. Perdue was appointed the first full time health officer of Norwalk, effective September 1. Norwalk is now the ninth city in Connecticut to be on a full time basis. Dr. William Sherman Randall has been appointed health officer of Shelton to fill the unexpired term of the late Dr. John E. Black. Dr. Donald J. McCrann, West Hartford, has succeeded Dr. Maurice B. Thompson as health officer of Bloomfield. Dr. Archibald M. Gaulocher, Wingdale, N. Y., is health officer of Kent and Dr. Frank D. Ursone, Norfolk, health officer of Colebrook. Dr. Edward J. Brophy is health officer of Norwich, filling the unexpired term of the late Dr. Harrison Gray.

### DELAWARE

**State Medical Election.**—Dr. Meredith I. Samuel, Wilmington, was elected president of the Medical Society of Delaware at its annual meeting in Dover October 12. Other newly elected officers are Drs. Bruce Barnes, Seaford, and Charles G. Harmonson, Smyrna, vice presidents; John H. Mullin, Wilmington, secretary, and Alfred L. Heck, Wilmington, treasurer.

### ILLINOIS

**New District Health Units.**—A new district health department has been established in Woodstock to serve the counties of Boone, Lake, McHenry and Winnebago. Dr. John F. Shronts is the district health officer.—Dr. Maurice Gore, Aurora, has been appointed medical officer in charge of the new health district embracing the counties of DeKalb, Grundy, Kane, Kendall and LaSalle. A new unit including Bond, Clinton, Madison and St. Clair counties has been placed under the direction of Dr. Claude Milton Eberhart, Highland.

### Chicago

**Personal.**—Dr. Paul C. Barton, since 1934 a member of the staff of the Council on Pharmacy and Chemistry, has been appointed Director of the Bureau of Investigation of the American Medical Association. Following graduation from the University of Maryland School of Medicine, Baltimore, and completion of his internship, Dr. Barton spent several years in private practice.—Mrs. Lucille Smith, director of

medical service for the Chicago Relief Administration, resigned October 6 to accept a position with the Social Security Board in Washington, D. C., newspapers reported.

**Symposium on Blood Transfusions.**—The Chicago Medical Society devoted its meeting November 9 to a symposium on blood transfusions. The following spoke:

Dr. Bernard Fantus, The Blood Bank of Cook County Hospital (Preserved Blood versus Fresh Blood).  
Dr. Elizabeth H. Schirmer, Blood Preservation Technic.  
Dr. Karl A. Meyer, Blood Transfusion Technic.  
Dr. Lindon Seed, Blood Transfusion Reaction.  
Dr. Egbert H. Fell, Transfusion of Fresh Blood.  
Dr. Josiah J. Moore, Practical Possibilities of Private Blood Banks.

### IOWA

**Symposium on Fractures.**—A symposium on fractures was presented before the Pottawattamie County Medical Society in Council Bluffs November 7 by the following:

Dr. Robert D. Schrock, Omaha, Fractures of the Ulna and Radius at the Wrist.  
Dr. Hiram Winnett Orr, Lincoln, Neb., Prevention and Control of Infection in Fractures and Other Bone Surgery.  
Dr. Arthur Steindler, Iowa City, Fracture Deformities of the Ankle.  
Dr. Karl R. Wernsdorff, Council Bluffs, Fractures of the Spine.  
Dr. Charles L. Scudder, Boston, Regional Fracture Committees of the United States and Fractures of the Os Calcis.

**Refresher Courses.**—Two refresher courses in obstetrics and pediatrics opened early in October in the eleventh and ninth councilor districts, under the auspices of the speakers' bureau of the state medical society, the State University of Iowa College of Medicine, Iowa City, the Iowa Pediatric Club, the Central Association of Obstetricians and Gynecologists and the state department of health. In the eleventh district the first two meetings were held in Atlantic, the next three in Red Oak, and the last three will be given in Harlan. The entire program for the ninth district is being presented in Chariton. The speakers include Drs. Everett D. Plass, John H. Randall, William F. Mengert, Philip C. Jeans, Julian D. Boyd, all of Iowa City; Robert M. Collins and Jack V. Treynor, Council Bluffs; Robert H. McBride, Sioux City, and Fred Moore, Des Moines.

### LOUISIANA

**Society News.**—At a meeting of the Orleans Parish Medical Society in New Orleans October 24 the speakers were Drs. Lucien A. LeDoux on influence and effects of toxemias on menstruation; Leon J. Menville, "Treatment of Advanced Carcinoma of the Cervix," and Robert H. Bayley and David E. Fader, "Congenital Cystic Lung Disease."—Dr. Harold R. Cummings, Los Angeles, gave a talk on Metchnikoff before the Tulane History of Medicine Society, New Orleans, October 21.

**Drive Against Illegal Practitioners.**—J. E. Garret was fined \$100 for practicing medicine without a license and \$1,000 for selling improperly labeled products in court at Abbeville recently; \$700 of the larger fine was suspended. Newspapers reported this as the first major conviction obtained by the state board of health in its drive against the illegal practice of medicine and the misbranding of preparations. It was also stated that forty manufacturers who had not registered with the board applied for certification of their products after recent seizure of eighteen uncertified products.

### MARYLAND

**Dr. Williams Reappointed Commissioner of Health.**—Dr. Huntington Williams has been reappointed commissioner of health of Baltimore for another term of six years. Dr. Williams first became commissioner Jan. 31, 1933, after having served as director of health from Oct. 1, 1931.

**Parrots Forbidden in Baltimore.**—The mayor and city council of Baltimore approved an ordinance October 3 prohibiting bringing into, offering for sale, selling, giving away or breeding within the limits of Baltimore parrots, parakeets, love birds, macaws, cockatoos, lorics, lorikeets and other birds of the psittacine family. The ordinance provides that zoologic gardens operated under public authority or laboratories in which scientific research is being carried out may receive or import birds of the psittacine family in conformity with such rules and regulations as prescribed by the city department of health.

**Society News.**—The Baltimore City Medical Society met with the Medical Society of the District of Columbia November 16 in Washington; the speakers were Drs. Edmund L. Keeney on "Slow Epinephrine"; Hugh H. Young, "Genital Abnormalities of Hermaphroditism and Related Adrenal Diseases," and Monte Edwards, "Rectal Lymphogranuloma."

Dr. William Barry Wood Jr. addressed the Baltimore society November 4 on "Treatment of Lobar Pneumonia." A symposium on vitamins was presented before the Baltimore society October 21 by Drs. Julius Friedenwald on "Gastrointestinal Aspects"; Paul W. Clough, "Neurologic Aspects," and Esther L. Richards, "Psychiatric Aspects."

### MICHIGAN

**Society News.**—Dr. James A. Conner, Chicago, addressed the medical section of the Wayne County Medical Society, Detroit, October 10, on "Treatment of Pertussis." The surgical section was addressed October 24 by Dr. Hans Finsterer, Vienna, Austria, on "Surgical Treatment of Acute Gallbladder Diseases and the Common Duct Obstructions."—Dr. Sabina Kessler-Frux, Bay City, was elected president of the Michigan branch of the American Medical Women's Association at the annual meeting in Detroit in September, succeeding Dr. Mary Margaret Frazer, Detroit.

**Course in Basic Ophthalmology.**—A new course in basic ophthalmology began November 1 at Wayne University College of Medicine, Detroit, to continue each Tuesday and Friday throughout the year. Designed for residents and those interested in increasing their basic knowledge in ophthalmology, the first course is on histology, comparative and human, while the second will be in physiologic optics, physiology of the eye, gross anatomic sections of the head and neck and so on. There is no fee for the courses. Dr. Parker Heath is professor and head of the department of ophthalmology.

**Changes in Health Officers.**—Dr. Philip E. M. Bourland, Lansing, recently associated with the state board of health, has been appointed director of the Dickinson County health unit, succeeding Dr. Clifton E. Merritt, Bay City, who accepted a similar position in Bay County. Dr. Russell E. Pleune, Lansing, who was scheduled to take over the post in Dickinson County, is now director of the health unit, succeeding Dr. Forrest J. . . . Dr. Guy R. Post, Fremont, has resigned as director of the Tri-County Health Unit, serving Newaygo, Lake and Oceana counties, effective September 15. Dr. Reuben J. Harrington, for fourteen years health officer of Muskegon, has been appointed in charge of the unit in Muskegon County, succeeding Dr. Richard Sears of the state department of health. Dr. Clifton C. Corkill, Ontonagon, director of the Ontonagon-Baraga counties health unit, has been appointed in charge of the Menominee County health department. He succeeds Dr. Lawrence A. Berg, Detroit, who is on a year's leave of absence to take a graduate course at the University of Michigan Medical School.

### MINNESOTA

**Research in Food Technology.**—An annual grant of \$25,000 has been given to the University of Minnesota by George A. Hormel and Company, Austin, to establish the Hormel Research Foundation for the promotion of researches in the field of food technology. According to Science, most of the research will be devoted to problems of importance to the packing industry. The work will be carried on by a committee consisting of George O. Burr, Ph.D., Ross A. Gortner, Ph.D., Halvor O. Halvorson, Ph.D., Walter M. Lauer, Ph.D., and Samuel C. Lind, Ph.D. Dr. Lind is chairman.

### NEW YORK

**Free Dispensary Fifty Years Old.**—The Syracuse Free Dispensary celebrated its fiftieth anniversary October 13. Rev. Alphonse M. Schwitalla, dean, St. Louis University School of Medicine, was the principal speaker, on "The Future of Dispensaries." Dr. Charles H. Benson, Bainbridge, for many years head of the dispensary and now retired, was a guest of honor.

**District Meeting.**—The annual meeting of the Fourth District of the Medical Society of the State of New York was held in Amsterdam September 30 and October 1. The speakers included Drs. Lyle A. Sutton, Albany, on "The Menopausal Syndrome"; Stafford L. Warren, Rochester, "Fever Therapy," and William Cook Spain, New York, "The Food Factor in Allergy."

**Society News.**—Forum discussions made up the program of the Onondaga County Medical Society, Syracuse, November 1. Dr. Brooks W. McCuen led a forum on "Cancer of the Rectum and Colon" with Drs. John C. M. Brust and Albert G. Swift as discussers. Dr. Joseph R. Wiseman led a discussion of "Peptic Ulcer," in which the participants were Drs. Clark J. Laus, Donald S. Childs and Percival K. Menzies. Members of the staff of the Syracuse Psychopathic Hospital

presented the program October 4: Drs. Carl A. Whitaker, on "Clinic Treatment of Syphilis of the Central Nervous System" and Eugene Davidoff, "Psychiatric Aspects of the Treatment of Orchidism" and "Play Technic in Children and Juveniles."

### New York City

**Appointments Available at Hospital for Joint Diseases.**—Six house staff appointments on the general service for two years rotating service are available at the Hospital for Joint Diseases, three to begin July 1, 1939, and three to begin Jan. 1, 1940. An examination will be held at the hospital Dec. 29, 1938, for which applicants must register before December 15. The hospital provides maintenance and uniforms. Graduating students and graduates (unmarried men) of class A medical schools are eligible. Applications should be addressed to the Director of the Hospital, Madison Avenue at One Hundred and Twenty-Third Street, New York.

**Position Open for Bacteriologist.**—The Municipal Civil Service Commission announces a vacancy for a bacteriologist. Applicants must have been citizens and bona fide residents of the city for three years. Requirements are an M.D. degree or a Ph.D. degree in bacteriology from an accredited institution, three years' experience in bacteriology, and in addition two years' specialized training in blood grouping and related serologic work or a satisfactory equivalent. Applications will be received until 4 p. m., November 25. Blanks may be obtained by writing to the commission with return postage enclosed. The address is room 1400, Municipal Building, Manhattan.

### NORTH CAROLINA

**Symposium at Duke University.**—More than 500 Southern physicians attended a symposium on medical problems presented by Duke University, Durham, October 13-15 as the first of a series of symposiums celebrating the university's centennial. After the welcoming address by William Preston Few, LL.D., president of the university, Drs. Allen Weir Freeman, Baltimore, and George W. McCoy, New Orleans, spoke on "Public Health Developments in the South" and "Leprosy in the United States" respectively. In the evening there was a discussion of "The Future of American Medicine" by Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, John P. Peters, New Haven, Conn., and Wingate M. Johnson, Winston-Salem. Dr. Milton J. Rosenau, professor of epidemiology, University of North Carolina School of Medicine, Chapel Hill, presided. Addresses were presented Friday morning October 14 by Drs. George H. Whipple, Rochester, N. Y., on "Anemia and the Building of Hemoglobin in the Body" and William H. Sebrell Jr. of the U. S. Public Health Service, Washington, D. C., on pellagra. In the afternoon the speakers were Drs. Charles F. Craig and Edward W. Alton Ochsner, New Orleans, on amebiasis and "The Surgeon's Contribution to Treatment of Amebiasis" respectively. The remaining addresses of the symposium dealt also with tropical diseases: Drs. William G. MacCallum, Baltimore, on "Malaria"; Arturo Lorenzo Carrion, University of Puerto Rico School of Tropical Medicine, San Juan, "Rising Significance of Fungus Infections in Man," and Albert M. Snell, Rochester, Minn., "Tropical and Nontropical Sprue (Chronic Idiopathic Steatorrhea): Their Probable Interrelationship." Dr. James Buren Sidbury, Wilmington, president of the Medical Society of North Carolina, presided at the Saturday morning session.

### OHIO

**The First Lower Lecture.**—The first lecture of a series made possible by the establishment of the Lower Fund was presented by Dr. Oliver H. Perry Pepper, Philadelphia, November 18 in the Medical Library Auditorium, Cleveland, on "Diverticulitis of the Colon." Dr. William E. Lower, Cleveland, endowed the lectureship recently, directing that it deal with some recent development or research but not be confined to any one branch of medicine.

**Personal.**—Dr. John C. Darby, Cleveland, was honored with a dinner September 22 marking his retirement from the 368th Medical Regiment of the Officers Reserve Corps, U. S. Army, of which he had been commander since 1929. He received an honorary life commission as colonel of the regiment. Colonel Darby saw service in the Spanish American War, on the Mexican border and in the World War in France. He was graduated from Western Reserve University School of Medicine in 1900.—Dr. Raymond S. Rosedale, St. Louis, has been appointed pathologist at Mercy Hospital, Canton, to succeed Dr. Max Shaweker.

**Society News.**—The Morgan County Bar Association entertained the Morgan County Medical Society October 11 in McConnellsville. The speakers were Dr. Roy J. Secrest, until recently assistant medical director of the state industrial commission; on the commission and the practicing physician; Mr. R. H. Edwards, claims referee of the industrial commission, on the expert medical witness, and Dr. William E. Masters, on the doctor as a witness.—Dr. Everett N. Collins, Cleveland, addressed the Portage County Medical Society, Ravenna, September 8, on diseases of the colon.—Drs. Charles A. Doan and Bruce K. Wiseman addressed the Columbus Academy of Medicine September 19 on "Advances in the Understanding, Differential Diagnosis and Treatment of the More Common Anemic States" and "Advances in the Diagnosis and Therapy of Thrombocytopenic Purpura" respectively.—Dr. William Bates, Philadelphia, addressed the Montgomery County Medical Society, Dayton, November 4, on "Differentiation Between Visceral and Parietal Pain." Drs. Thomas E. Newell and Miles T. Hoerner addressed the society October 7 on "Etiology and Differentiation of Jaundice" and "Surgical Treatment of Lesions Producing Jaundice" respectively.

### OREGON

**Personal.**—Dr. Thomas L. Meador, Portland, has been appointed in charge of the division of communicable disease in the city department of health.

**New Orthopedic Club.**—Physicians in Portland who limit their practice to orthopedic surgery formed the Portland Orthopedic Club at a meeting October 21. Dr. Otis F. Akin was made president and Dr. Alfred Gurney Kimberley, secretary. Candidates for membership must be diplomates of the American Board of Orthopaedic Surgery.

**The Widmer Research Fund.**—The University of Oregon Medical School, Portland, has received a gift of 171.67 acres of land near Eugene valued at about \$30,000, the income from which is to be devoted to research in cancer and heart disease. The property was conveyed by Misses Gertrude and Margaret Widmer, Eugene, in memory of their parents and of two brothers who graduated from the university. The gift will be established as the Widmer Memorial Research Fund.

**Annual Registration Due December 1.**—All practitioners of medicine and surgery holding licenses to practice in Oregon are required by law to register annually on or before December 1 with the secretary of the Board of Medical Examiners and at that time to pay a fee of \$5. A practitioner failing to register is subject to a penalty of \$1 for each thirty days or part thereof of default, and his failure to reregister within ninety days after December 1 is a misdemeanor.

### PENNSYLVANIA

**Society News.**—A symposium on typhoid fever was presented before the Fayette County Medical Society, Uniontown, November 3, by Drs. Charles H. Smith, Herbert Lund and John B. Hibbs, all of Uniontown, and Paul A. Keeney, Harrisburg.—Dr. Morris A. Silver, Harrisburg, addressed the Dauphin County Medical Society, Harrisburg, November 1 on "Recognition of the Commoner Anorectal Diseases and Their Treatment."—Dr. Daniel Murray Angevine, New York, addressed the Harrisburg Academy of Medicine recently on arthritis.—Dr. Albert F. Doyle, Johnstown, addressed the Montour County Medical Society, Danville, October 21 on "Public Health Duties of the Physician Treating Syphilis."

### Pittsburgh

**Auxiliary Holds Annual Institute.**—The Woman's Auxiliary of the Allegheny County Medical Society held its annual health institute at the William Penn Hotel November 1. Dr. Paul Titus gave an address on maternal conditions in the United States, followed by a showing of the "Birth of a Baby." Dr. Chauncey L. Palmer, chairman of the committee on public health legislation of the state medical society, spoke on "Health Legislation—What State Medicine Means to You." Mrs. Joseph P. Dobo spoke on "State Medicine as I Knew It in Vienna." Dr. John N. Frederick discussed "Mental Diseases with Special Reference to Causes and Prevention," and Dr. William H. Guy presented an illustrated lecture on syphilis.

**Society News.**—Dr. Claude S. Beck, Cleveland, was the guest speaker before the Allegheny County Medical Society November 15 on "Heart Surgery." A. L. Murray of the U. S. Bureau of Mines, Pittsburgh, addressed the society October 18 on "Carbon Monoxide Poisoning" and Dr. Moses Paulson, Baltimore, "Diarrheas and Dysentery of the Adult

—Practical Aspects of Diagnosis and Treatment." The scientific exhibit was presented by the Bureau of Mines. There was also a discussion on "Reaching the Ear of the Health and Tax Conscious Public Through the Membership of the County Medical Society and Its Woman's Auxiliary" by Mrs. Augustus S. Kech, Altoona, chairman of the public relations committee of the Woman's Auxiliary to the Medical Society of the State of Pennsylvania. Other speakers were Drs. Chauncey L. Palmer, chairman of the committee on legislation of the state medical society; Charles H. Henninger, president-elect, and Mrs. Walter F. Donaldson, Pittsburgh, president of the Woman's Auxiliary of the state medical society; all are of Pittsburgh.—Drs. George Booth and Karl Zimmerman addressed the Pittsburgh Academy of Medicine October 25 on "Hypoglycemia" and "Oil Soluble Anesthetics in the Treatment of Anal Ulcer" respectively.

### TENNESSEE

**District Meeting.**—Guest speakers at the annual meeting of the Third Councilor District of the Tennessee State Medical Association in Chattanooga, September 29, were Drs. Hugh H. Trout, Roanoke, Va., on "Some Mistakes in the Diagnosis of Acute Appendicitis" and "Treatment of Carcinoma of the Breast"; Axel N. Arneson, St. Louis, "Carcinoma of the Cervix" and "Carcinoma of the Uterus," and John B. Youmans, Nashville, "Less Common Manifestations of Coronary Thrombosis" and "Recognition of Cardiac Arrhythmias by Simple Physical Examination."

### VIRGINIA

**Special Society Elections.**—Several special societies held their annual meetings in Danville during the annual session of the Medical Society of Virginia in October. The Virginia Orthopedic Society elected the following officers: Drs. Roy M. Hoover, Roanoke, president; Henry H. Wescott, Roanoke, vice president, and Bernard H. Kyle, Lynchburg, secretary, reelected. Dr. William W. Waddell Jr., Charlottesville, was elected president of the Virginia Pediatric Society; Dr. Leta J. White, Petersburg, vice president, and Dr. John M. Bishop, Roanoke, reelected secretary. At the meeting of the Virginia Obstetrical and Gynecological Society the following were elected: Drs. Charles J. Andrews, Norfolk, president; Harry Hudnall Ware Jr., Richmond, vice president, and Richard B. Nicholls, Norfolk, secretary. The Virginia Radiological Society reelected Drs. Frederick M. Hodges, Richmond, president, and Vincent W. Archer, Charlottesville, secretary. Dr. Lawrence T. Price, Richmond, was elected president of the Virginia Urological Society; Drs. Albert A. Creecy, Newport News, and Linwood D. Keyser, Roanoke, vice president and secretary respectively.

### WASHINGTON

**State Program for Crippled Children.**—During the first two years of the state crippled children's program conducted by the Washington State Department of Social Security with state and federal funds, 1,940 children have attended clinics. These clinics have been held at intervals of six months in six centers, and twenty-three orthopedic and plastic surgeons have assisted in them. Of the children, 731 have been referred to the state agency and 309 to private orthopedic units for treatment. The staff surgeons elected from their group seven men to serve as a committee to review cases referred to the crippled children's program and assign them for treatment to the staff surgeons in the hospital center nearest each child's home. The social workers in the hospital centers cooperate in arranging convalescent care and educational facilities. If the child when discharged from orthopedic treatment is of the age of employment but not equipped to enter private industry, he is referred to the state department of vocational rehabilitation for possible training and placement. Since September 1935 the state has spent \$118,730.96 in the program and the Children's Bureau contributed \$109,354.82.

### WISCONSIN

**Society News.**—Drs. Stanley R. Maxeiner and Henry E. Michelson, Minneapolis, addressed the Barron-Washburn-Sawyer-Burnett County Medical Society in Rice Lake, October 4, on "Surgery of the Stomach and Duodenum" and "Diagnosis and Treatment of Common Skin Diseases" respectively.—Dr. Raymond G. Arveson, Frederic, president-elect of the State Medical Society of Wisconsin, addressed the Chippewa County Medical Society, Chippewa Falls, October 25, on "Adequacy of Medical Care."—At a meeting of the Grant County

Medical Society, Lancaster, October 25 the speakers were Drs. John C. Grill, Milwaukee, on "Importance of the Laboratory in the Diagnosis of Blood Diseases"; Elmer L. Sevringhaus, Madison, "Menopause and Irregular Menstruation," and George H. Ewell, Madison, "Interesting Urological Cases." Mr. J. George Crownhart, executive secretary of the State Medical Society of Wisconsin, Madison, reported on his recent study of sickness care in Europe.—Dr. Henry W. Meyerding, Rochester, Minn., addressed the Kenosha County Medical Society, Kenosha, September 22 on recent advances in orthopedics.—Dr. James M. Hayes, Minneapolis, addressed the La Crosse County Medical Society October 12 on "Acute Abdominal Surgery" and Dr. Albert E. Rector, Appleton, president of the state medical society, discussed "Present Day Trends in Medicine."

### GENERAL

**Examinations in Pediatrics.**—The American Board of Pediatrics announces that its 1939 examinations will be held April 26 in New York, May 16 in St. Louis, and November 14-15 in Cincinnati. Appointments for the April examinations must be made by December 26, for the May one by Jan. 16, 1939, and for the November one by July 14. The secretary is Dr. Charles Anderson Aldrich, 723 Elm Street, Winnetka, Ill.

**The Lilly Award in Biologic Chemistry.**—Nominations are invited for the Eli Lilly and Company Prize in Biological Chemistry to be awarded by the American Chemical Society at its spring meeting. The prize, established by the Lilly firm in 1934, is \$1,000 with a bronze medal and \$150 or as much thereof as is needed to defray the expenses of the recipient to the meeting. A nominee must not be over 35 years old on April 30 of the year of the prize and shall have accomplished outstanding research in biologic chemistry, working in a college or university. For the purpose of this award biologic chemistry does not include immunology, clinical investigation, pharmacology or experimental therapeutics. It is intended for persons on the threshold of their career and will not be judged in comparison with the work of more mature and experienced chemists. Nominations must be received before Jan. 5, 1939. They should be sent directly to the secretary of the American Chemical Society, Charles L. Parsons, Mills Building, Washington, D. C.

**Bequests and Donations.**—The following bequests and donations have recently been announced:

Christ Church Hospital, Philadelphia, \$7,800 by the will of Sarah L. Bailey.

Fitzgerald-Mercy Hospital, Darby, Pa., \$5,000 by the will of the late Mrs. May Neff Fitzgerald Major, whose first husband bequeathed funds for the erection of the hospital; Children's Seashore Home, Atlantic City, N. J., also received \$1,000.

Mount Sinai Hospital, New York, \$10,000 by the will of the late Mrs. Carrie L. Lehman.

Methodist Episcopal Hospital, Indianapolis, \$10,000 by the will of Lulu E. Critz, Anderson, Ind., who died June 29.

American Society for the Control of Cancer, New York, \$10,000 by the will of Miss Katherine Rhoads, Richmond, Va., to be used in Virginia.

Hamot Hospital Association, Erie, Pa., and Wills Hospital, Philadelphia, \$1,000 each by the will of Frank B. Rutherford.

Mansfield General Hospital, Mansfield, Ohio, \$25,000 from the estate of the late Richmond Smith.

Lake County Memorial Hospital, Painesville, Ohio, \$5,000 from the estate of the late Clifton N. Windecker.

Bronson Methodist Hospital, Kalamazoo, Mich., \$100,000 from the Kresge Foundation to be applied on a new addition.

The city of Coshocton, Ohio, will receive about \$225,000 from the will of Ernest A. Bachert, to be held in trust for ten years and to be expended at the end of that period for the erection and maintenance of a hospital for crippled children.

Harrisburg Polyclinic Hospital, Harrisburg, Pa., \$350,000 by the will of the late Daniel M. Dull in memory of his father.

**Society Elections.**—Dr. James R. McCord, Atlanta, Ga., was chosen president-elect of the American Association of Obstetricians and Gynecologists at the recent annual meeting and Dr. James E. King, Buffalo, was installed as president-elect. Dr. James K. Quigley, Rochester, N. Y., was elected vice president and Dr. James R. Bloss, Huntington, W. Va., was reelected secretary. The next meeting will be held in Hot Springs, Va.—Dr. Harold D. Corbusier, Plainfield, N. J., was elected president of the Academy of Physical Medicine at the annual meeting in Washington, D. C., in October. Drs. Fred H. Albee, New York, and William H. Schmidt, Philadelphia, were elected vice presidents and Dr. Herman A. Osgood, Boston, was elected secretary.—Dr. Russell H. Oppenheimer, Atlanta, was chosen president-elect of the Association of American Medical Colleges at its annual meeting in Syracuse, N. Y., October 24-26, and Dr. Willard C. Rappleye, New York, was installed as president. Dr. Waller S. Leathers, Nashville, Tenn., was elected vice president and Dr. Fred C. Zapffe, Chicago, reelected secretary. The next meeting will be held in Cincinnati, Oct. 23-25, 1939.

**Radiological Society of North America.**—The annual meeting of the Radiological Society of North America will be held in Pittsburgh November 28-December 2 with headquarters at the William Penn Hotel. This year the society is sponsoring its first refresher courses, which will be given November 27-28 in the physics of radiation, radiology of the chest, radiology of the gastrointestinal tract, pathology of tumors, radiology of bone tumors, roentgen analysis of fractures, and radiology of sinuses and mastoids. Much of the scientific program is in the form of symposiums. Among the speakers will be:

Drs. Marcy L. Sussman and Leopold Jachas, New York, Bone Changes in Generalized Lipoid Diseases.

Drs. Ross Golden and Paul C. Swenson, New York, Experiences with the Compression Technic in Gastrointestinal Examinations.

Dr. Milton Friedman, New York, The Relation of Ovarian Hormones to Benign Breast Hyperplasia and Neoplasia.

Dr. Vincent C. Johnson, Ann Arbor, Mich., The Value of Roentgen Examination of the Paranasal Sinuses.

Drs. David E. Ehrlich and Arthur B. Robins, New York, Group X-Ray Surveys of Apparently Healthy Individuals.

Dr. Herman A. Osgood, Boston, Treatment of Acute and Chronic Inflammatory Conditions by Fractional Doses of X-Rays.

Dr. John D. Camp, Rochester, Minn., Experiences with Lipiodol in the Localization of Lesions Associated with Low Back and Sciatic Pain.

Dr. Arthur U. Desjardins, Rochester, Minn., Roentgen Therapy for Chronic Infectious Arthritis.

Dr. Hugh M. Wilson, New Haven, Conn., Exploration of the Thorax with Body Section Roentgenography.

Dr. Henri Coutard, Chicago, Present Conception of Treatment of the Larynx.

**Changes in Status of Licensure.**—The Ohio State Medical Board recently reported the following action:

Dr. Charles R. Buck, Cincinnati, license restored July 19.

Dr. Ralph Bernard Brown, Columbus, license restored April 5.

The New York State Board of Medical Examiners has recently reported suspension of licenses of the following physicians on the basis of fraud and deceit:

Dr. Isadore Roth, Brooklyn, one year from June 17.

Dr. Benjamin M. Wax, New York, one year from June 17.

Dr. Peter Kleinkopf, New York, eight months from June 17.

Dr. Isidore E. Kaplan, New York, one year from June 17.

Dr. Harry Grodzicker, Brooklyn, one year from June 17.

Dr. Max Ehrenberg, New York, one year from June 17.

Dr. Jacob R. Firneno, Brooklyn, six months from June 17.

The state board of medical education and licensure of Pennsylvania recently reported the following:

Dr. Arthur H. Gaston, Pittsburgh, license revoked for unethical conduct.

Dr. Harry Emerson Gray, Zelienople, license revoked for unethical conduct. It is said that although he had been a general practitioner for many years he posed as an eye specialist for an optical company.

The state department of registration of Utah reports the following action:

Dr. Afton M. Livingston, Ogden, license suspended August 1 for unprofessional conduct; to be reinstated in one year on condition that he complete a graduate course in a medical college.

The Florida State Board of Medical Examiners reports the following:

Dr. Roy Webb, Delray Beach, license restored June 13.

## Government Services

### Examination for Position of Toxicologist

The U. S. Civil Service Commission announces that an open competitive examination will be held for the position of principal industrial toxicologist (organic compounds) in the U. S. Public Health Service at a salary of \$5,600 a year. The duties will be to serve as scientific head of a section of industrial toxicology, studying the relation between chemical composition and pharmacologic action of organic compounds, and to be responsible for the planning and direction of scientific research and routine work in the industrial toxicology of organic compounds. Candidates must have graduated with an M.D. degree from a medical school of recognized standing and must not have passed their fifty-third birthday on the date of the close of applications. Applications and further details may be obtained from the Secretary, Board of U. S. Civil Service Examiners, at any first class post office, from the commission at Washington, D. C., or from the district office of the commission in any of the following cities: Atlanta, Boston, Chicago, Cincinnati, Denver, New Orleans, New York, Philadelphia, Seattle, St. Louis, St. Paul, San Francisco, Honolulu, Balboa Heights, St. C. Z., and San Juan, P. R. The closing date for applications is November 28, if received from states other than Arizona, California, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington and Wyoming. For the Far Western states the date is December 1.

## Foreign Letters

### PARIS

(From Our Regular Correspondent)

Oct. 22, 1938.

#### Action of Ephedrine in Acute Pancreatitis

At the July 8 meeting of the Société médicale des hôpitaux of Paris, a paper was read by Dr. P. Jacquet and his associates on three cases presenting a syndrome commonly observed in the initial stage of an acute pancreatitis. The existence of such an acute pancreatitis was verified at operation in two of the three cases. The clinical picture was identical, the noteworthy features being severe epigastric pain radiating toward the back, which could not be relieved by relatively large doses of morphine. The patients were pale and appeared to be in a state of shock with only slight increase in the pulse rate and no change in the blood pressure. There was a noticeable increase in the blood sugar content and a marked glycosuria in one patient. Ephedrine was given to all four patients to combat the symptoms of shock. In the first case 0.04 Gm. was given daily for three days and was followed by considerable relief of the pain. This patient was operated on successfully later for a hemorrhagic cyst of the pancreas. In the second case the symptoms of acute pancreatitis were accompanied by a hemorrhagic pleurisy. After a few days administration of 0.08 Gm. daily of ephedrine hydrochloride the abdominal pain, shock and pleurisy disappeared, but the pain recurred as soon as the ephedrine was discontinued. After the first dose was repeated the pain ceased. This patient was given a total of almost a gram of ephedrine hydrochloride in twenty-five days and never had a recurrence of symptoms during a year of observation. The third patient was given 0.04 Gm. of ephedrine hydrochloride in a single dose six hours after the onset. The pain and symptoms of shock disappeared but recurred two hours later. A second injection was given thirteen hours after the onset and again gave relief for two hours. A suprapubic incision revealed a hemoperitoneum but the patient's condition did not permit exploration of the upper portion of the abdomen. Recovery followed and no relapse was observed during the next three months. The conclusions based on these observations were that, before the irreparable lesions incident to an acute pancreatitis appear, there is a vascular disturbance on which such factors as the pharmacodynamic action of ephedrine, the shock of an operative intervention or perhaps a general anesthesia seem to have an inhibitory action. Ephedrine ought to be given in much larger doses in acute pancreatitis than in collapse or surgical shock. In the discussion, Dr. Gilbert-Dreyfus cited a case in which operation based on the diagnosis of acute peritonitis revealed an edema of the pancreas. Following the operation, repeated emesis and a poor general condition but no signs of circulatory collapse were noted. The patient was given 0.06 Gm. of ephedrine hydrochloride followed by complete transformation of the clinical picture after the fourth injection. Dr. Donzelot believed that pancreatic lesions were not always responsible for such a severe syndrome. The striking features in the pancreaticosolar syndrome were severe lumbar pain and very marked symptoms of shock.

#### Prolongation of Effects of Tetanus and Diphtheria Antitoxins

Prof. G. Ramon of the Pasteur Institute of Paris has studied the action of tetanus and diphtheria toxoids since his discovery of both these toxoids about ten years ago. At the July 8 meeting of the Société médicale des hôpitaux of Paris, Prof. Ramon and associates presented the results of the comparative effects of these toxoids in the form of two papers. They recalled their experience in the combined use of the tetanus

antitoxin and toxoid in vaccination against tetanus, a method now obligatory in the French army. The person to be vaccinated is given in two different places of the body a dose of the serum, for adults, representing from 10 to 20 thousand antitoxic units and another of 1 cc. of tetanus toxoid. Fifteen days later, 2 cc. of the toxoid is given and again three weeks after the second dose a third one of 2 cc. of the toxoid. The immunity conferred by the antitoxin is thus greatly prolonged. This combined use of the tetanus antitoxin and toxoid was utilized in the treatment of four cases of injuries as a prophylactic measure, the theory being that the serum, owing to its high titer in antitoxic units, had a better immediate protective action but that, because such action was only transitory, it could be prolonged by giving the tetanus toxoid. Each patient received a dose of the serum corresponding to 150,000 units and at the same time he was given 2 cc. of the tetanus toxoid. Later on, doses of 3, 4 and 5 cc. of the toxoid were given at intervals of a few days. Determinations of the antitoxin content of the blood made at various periods showed that it was possible to prolong the passive immunity conferred by the antitoxic serum, which is only of brief duration, by the active immunity due to the toxoid, which after repeated injections becomes more and more permanent. The great advantage of such a combined use of the antitetanus serum and tetanus toxoid is that not only will it be possible to avoid, in the future, the continued administration of large doses of the serum to prevent a late tetanus but the antitoxin units in the blood will be maintained at a sufficiently high titer, when the passive but transitory action of the serum is prolonged, through the active immunizing action of the toxoid. Up to the present, no untoward effect of the use of the toxoid has been reported.

In the second paper Professor Ramon discussed the first results of combined use of diphtheria antitoxin and toxoid. Although the use of the diphtheria antitoxin had revolutionized the treatment of the disease, the effects of the antitoxin in diphtheria conferred only a passive immunity of relatively short duration, so that it has become necessary to repeat the injections in order to prevent serious complications and recurrences. The object which Ramon had in mind in advocating the combined use of the diphtheria antitoxin and toxoid was to avoid giving additional doses of the former. Two injections are given in different parts of the body, one of a massive dose of the antidiphtheria serum, in general from 1,000 to 2,000 units per kilogram of weight, according to the severity of the case, a total of from 10 to 60 thousand units except in very grave cases, in which a dose of 80 thousand units is given. The dose of diphtheria toxoid should be 0.1 cc., representing 150 units. Following this large initial dose of the diphtheria antitoxin, the toxoid is injected at intervals of five days in progressively increasing doses, beginning with 1 cc., then 2 cc., 3 cc. and so on. This technic has been used by various clinicians in 120 cases of diphtheria with but slight reactions to be ascribed to the injections of the toxoid. Only three slight and transitory paralyses of the soft palate have been observed. A study of the titer of antitoxin units in the blood of these patients has shown that the transitory passive immunity conferred by the diphtheria antitoxin is converted into a prolonged active immunity as the result of the action of the toxoid.

In the discussion of the second paper, fifteen cases treated by this method were reported by Professor Debré and Dr. Mallet, who stated that their observations as to the transition from a passive immunity of short duration conferred by the diphtheria antitoxin to the prolonged active immunity conferred by the anatoxin entirely corroborated the report made by Professor Ramon. The number of cases, only fifteen, thus far treated was too small on which to base any opinion. Although no postdiphtheritic paralysis had been observed, the cases had been of a mild type. The allergic reactions due to the use



of the toxoid had been slight. Dr. Marquezy doubted whether Ramon's method offered any real advantages because nearly all patients who have been given the antitoxic serum show a protective titer of antitoxic units in the blood. The most important question in the treatment of diphtheria was to create as large a number of antitoxic units in the blood as possible and at as early a stage as it could be accomplished.

#### Basal Metabolism in Leukemia and Splenomegaly

Two papers on basal metabolism in leukemia and splenomegaly were read at the July 8 meeting of the Société médicale des hôpitaux by Drs. Emile Weil, hematologist, and A. Aschenasy. In fifteen cases of leukemia, five of which were of the myelogenous and ten of the lymphatic type, a persistent increase in the metabolic rate, which varied from 50 to 60 per cent, was observed in all the patients. This increase is independent of the number of red blood cells and the percentage of immature forms of red blood cells as well as of the size of the spleen or of the lymph nodes. The increased rate of basal metabolism is the expression of the entire leukopoietic process of the organism. A severe concomitant anemia appears to counteract the effects of the leukemia by lowering the metabolism rate. Although the latter may not have any prognostic value in the leukemias, it is of diagnostic interest in the cryptoleukemias involving the lymph nodes or spleen, in which the metabolic rate is constantly high. They had never observed any beneficial influence from irradiation of the thyroid.

As to the metabolic rate in splenomegaly, only a slight increase was noted in four cases of congenital hemolytic icterus, but a more marked increase in hypertrophic cirrhosis of the liver with splenomegaly. In three cases of Gaucher's disease and even in most cases of isolated splenomegaly, especially those of tuberculous or syphilitic origin, the metabolic rate was found to be about normal as opposed to the increased rate found in splenic cryptoleukemias and in splenohepatomegaly as observed in the erythroblastic form of adults. The rate was considerably increased in both of these types of blood disease. Whenever a high metabolic rate is accompanied by splenomegaly without icterus or acute posthemorrhagic anemia, the clinician must keep in mind the possible existence of a leukemia or of an erythroblastosis. Following splenectomy, a decrease of the metabolic rate was observed in three of four patients and an increase in a fifth one. The authors were of the opinion that the spleen has a constant influence on the metabolic rate but that this influence is subject to variations in individual cases.

#### BERLIN

(From Our Regular Correspondent)

Oct. 10, 1938.

#### The Pathology of Poliomyelitis

Dr. Peters of Munich had the opportunity to study the central nervous systems of thirty-nine persons who had died of poliomyelitis in 1937. Poliomyelitic changes were observed in the anterior horns of the spinal cord, in the lateral and posterior horns, in the region of the sensory and vegetative nuclei of the medulla and the pons, in the mesencephalon, in the hypothalamus, in the cerebellum and in various parts of the cerebral cortex (ascending frontal convolution, parietal cortex, insular cortex). In the ascending frontal region pathologic changes had occurred in all the layers, not merely in the third, fourth and fifth layers. In a few cases circumscribed foci, confined to the molecular layer of the frontal central cortex, were observed. Alterations were present throughout the central nervous system: ganglion cells were destroyed and glial-mesodermal infiltrates had formed. The degeneration of ganglion cells was most remarkable in the frontal horns of the spinal cord. In the cadavers studied the substantia nigra was relatively free from pathologic processes; in only a few instances had destruction of ganglion cells taken place therein. This observation is of twofold practical signifi-

cance: first, it is important to the anatomist for differential diagnosis of poliomyelitis and lethargic encephalitis (Economo) and it is important to the clinician, as he need not fear in general the manifestation of parkinsonian symptoms in persons who have recovered from poliomyelitis. In several cases thick glial-leukocytic infiltrates were found in the pons and in addition a deficiency of ganglion cells at the base of the pons in the vicinity of the pontile nuclei and the area of the pyramidal tract. These foci, together with foci in the ascending central region of the cerebral cortex, can through stimuli or trophic disturbances in the first motor neuron lead to spastic symptoms such as exaggerated reflexes. The latter symptom is more often determined in clinically examined cases. In three cadavers a manifest preponderance of pathologic changes in the brain, especially in the pons and medulla, as contrasted with the spinal cord, were noted. It may be assumed therefore that some cases of poliomyelitis, at least in the initial stage, present only lesions in the cerebral nerves, whereas not the slightest degree of paralysis is present in the region of the extremities; under certain circumstances spastic symptoms may even appear. In a few cases also more or less extensive primary foci were observed in the white substance of the spinal cord. The meningeal lesions, which in some instances consisted of a pronounced maculating, leukocytic meningitis, were interpreted as a primary reaction to poliomyelitis virus and its toxin. An interdependence of the meningeal changes and those in the nerve tissue does not exist; it is a question of coordinated processes. The wide distribution of the pathologic changes in poliomyelitis argues against use of the designation "poliomyelitis anterior." Heine-Medin disease is a myelo-encephalomeningitis which cannot rightfully be qualified by the adjective "anterior."

#### Sugar and the Teeth

Dr. Wolinz discusses the interrelation of sugar and the teeth in the *Zahnärztlichen Mitteilungen*. Statistics have revealed the astonishing fact that Germany, although a large producer of beet sugar, ranks fifth among the nations as a consumer of sugar. The view that sugar damages the teeth is no longer tenable on the basis of recent observations. Laboratory experiments as well as observations *in vivo* show that raw sugar and even mixtures of raw sugar and fat (whipped cream, marchpane) and protein exert no corrosive effect on the dental enamel. The injurious effect of neutral yeasty bakery goods can be favorably offset or abolished by ingestion of fruits and vegetables or salads. Carbohydrate ingested in the form of sugar ferments not at all or only as lactic acid. On the contrary, carbohydrate decomposes if ingested in the form of starches; it is first decomposed into sugar by the oral secretions and then undergoes further changes which exert a more harmful influence on the dental enamel than lactic acid. Dental caries among bakers is a special instance; particles of flour and sugar are inhaled in the course of the work; these particles light on the front teeth, and the deposits on the upper jaw in particular are not carried away by the saliva. Workers in sugar are consistently free from sugar caries.

#### Prof. Johannes Lange Is Dead.

With Prof. Johannes Lange, ordinarius in psychiatry at Breslau, passes at the age of 47 one of the finest of the younger German psychiatrists. Lange was a pupil of Kraepelin in the best sense of the word; he was loyal to his teacher and possessed the latter's eagerness for achievement. Lange's energetic pursuit of research and his remarkably able presentation of material quickly smoothed the path of his academic career; at the age of 40 he was already ordinarius. In addition to his particular specialty, Lange concerned himself professionally with cerebral pathology and genetic research and contributed notably to those fields. One has only to recall his research on twins, studies which resulted in the volume "Crime as Destiny," Precisely in this controversial field of genetic research, in which at present

so many differently minded elements are mixed, Lange has accomplished much good through public criticism of exaggerations and spurious representations, no mean task in view of the difficult situations often encountered in this field today.

### AUSTRALIA

(From Our Regular Correspondent)

Oct. 12, 1938.

#### Prophylaxis of Gas Gangrene

A material suitable for immunizing man against gas gangrene due to *Bacillus welchii* has been described by Penfold and Tolhurst at the Baker Institute, Melbourne. These workers have previously described the immunization of animals with alum-precipitated formaldehyde toxoid made from *Bacillus welchii* toxin, and their experiments with animals have been so successful that in August 1937 it was decided to use the vaccine in man. An eighteen hour culture of *Bacillus welchii* grown in anaerobic veal broth containing 0.1 per cent of dextrose was filtered through a Seitz bacterial pad and the minimum lethal dose of the filtrate was determined intraperitoneally in mice. About 0.4 per cent of solution of formaldehyde was added to a freshly prepared toxin and the mixture was incubated at 37 C. for six or seven days, until the toxicity was so reduced that 1 cc. would not kill mice weighing 20 Gm., while 5 cc. would kill rats weighing 100 Gm. The toxoid was precipitated with an 8 per cent solution of alum and the immunizing power of the material was tested in guinea pigs. The first human subject received 0.25 and 0.5 cc. subcutaneously, with an interval of four weeks between the doses. The reactions were mild and restricted to the site of inoculation. Further injections in different persons with doses up to 1 cc. caused no serious reactions. Examination of immunity response showed that this alum-precipitated *Bacillus welchii* toxoid given in two or three injections stimulated the production of antitoxin in all the persons injected. To demonstrate that the immune human serum was fully protective against living *Bacillus welchii* culture, passive immunity experiments were carried out in mice. It was found that the protected mice withstood at least two minimum lethal doses of culture. It has not yet been determined what level of antitoxin is fully protective or what is the duration of the immunity in man.

#### Physical Fitness Campaign

Australia has lagged behind certain other countries in attempting to improve the health and physique of her people by engaging in an intensive campaign of public education in physical fitness. It is encouraging that several of the state governments have taken steps this year in such a direction. At a meeting of the delegates from sporting bodies with a commonwealth-wide representation held in Sydney following this year's Olympic Games, it was agreed that there was urgent need for a fitness campaign in Australia. This feeling coincides with a similar development in medical and scientific circles, and plans for the institution of such a campaign is now under consideration in most states. One difficulty is the scarcity of qualified instructors who are fully acquainted with modern methods in physical training now in practice abroad. A welcome indication of progress is the appointment of a Canadian expert to the position of director of physical education in New South Wales, which state is furthest advanced in the fitness movement. Its government has appointed a physical education advisory committee to recommend methods adapted to local circumstances and the character and ideals of the community which can be adopted in New South Wales. It is hoped that sporting organizations, medical societies and other scientific bodies will cooperate fully in this movement which has found life in Australia this year. Fortunate as we are in the matter of low death rates and facilities for enjoying

the benefits of open air games, there is manifest scope for the avoidance of much sickness which would yield to a better understanding by the people of the functioning of their bodies.

#### Insurance Difficulties in New Zealand

New Zealand, as well as Australia, is experiencing some difficulty over the question of cooperation between the medical profession and the government on matters pertaining to health insurance. The British Medical Association in New Zealand, feeling that the government's proposed scheme for a universal practitioner service offered no appreciable advantage over the system that obtains at present, submitted to the government an alternative scheme for a more complete service based on income limits. The New Zealand government rejected this scheme, and as a result the association has broken off all discussions with the government. This difficulty with the medical profession is not the only problem met by the government in its attempt to introduce its social security plan. For several months a special committee has been investigating financial aspects of the whole scheme, without reaching any satisfactory decisions.

#### Tests of the Milk Supply

The announcement that, in future, regular monthly bacteriologic tests will be made of Melbourne's milk supply marks a progressive step in the development of Australia's public health activities. This is the first regulation of its kind in Australia. Under the plan, milk from every farm supplying the metropolitan area will be subjected to a test once a month. The work will be carried out by officers of the department of agriculture, the cost being met by the milk board. These tests will give metropolitan consumers definite assurance of a clean and safe milk supply, and it is expected that this assurance will stimulate the consumption of milk—a result desirable from the medical as well as the producers' standpoint, as the consumption of milk in Australia, notwithstanding the fact that dairying is one of its most important industries, is far below an adequate requirement for optimal health.

#### Gift for China

The Australian government has provided 500,000 doses of anticholera serum as part of a world gift of 6,000,000 doses to aid China in fighting her present epidemics of cholera. The serum was prepared by the commonwealth laboratories and is valued at approximately £4,000.

#### Death of Sir Colin MacKenzie

The death of Sir William Colin MacKenzie, M.D. (Melbourne), F.R.C.S. (Edinburgh), F.R.S. (Edinburgh), the founder and first director of the Australian Institute of Anatomy at Canberra, means a definite loss to the medical profession of Australia. Sir Colin belonged to that small band of Australian medical men whose work and writings are known beyond the confines of our island continent. He had a most unusual professional career, graduating as a comparative anatomist from the ranks of general practitioners of medicine. One of his earliest studies was on syphilitic dactylitis, and for two years before Schaudinn's momentous discovery of the spirochete of syphilis he urged the officers of the bacteriologic department of the University of Melbourne to collaborate with him in a search for the causal organism. During his first visit to Europe in 1904, MacKenzie was greatly influenced by the principles of muscle rest and muscle recovery then finding a place in orthopedic treatment. On his return to Melbourne the treatment of the recent and remote effects of infantile paralysis on children was the master idea in his mind. He gradually evolved his theories relating to the fascinating subject of muscle reeducation. These slowly took shape until they were ultimately embodied in his textbook "The Action of Muscles, Including Muscle Rest and Muscle Reeducation." Although commonplace today, MacKenzie's original concep-



tions were then revolutionary. He was the first to use the special term "muscle reeducation" and to stress the importance of the action of gravity in all educational attempts to regain muscle function after paresis of any nature. The minimal load, the zero position, the smooth powdered surface of board or cardboard for reeducational muscle work must always be associated with his name. While an orthopedic surgeon he found time to investigate the special anatomic problems associated with native fauna in Australia. These dissections helped him to correlate function and structure in muscles and to develop treatment for paralyzed muscles accordingly. After the great war MacKenzie devoted himself more and more to comparative anatomy, and his collection of Australian faunal specimens eventually became too great for any private individual. The commonwealth government acquired the collection as a gift to the nation in 1924. Subsequently William Colin MacKenzie received the honor of knighthood. In 1930 the collections were transferred to Canberra and have since been housed, with many additional gifts, in the two spacious museums attached to the Australian Institute of Anatomy. Here, as director, Sir Colin spent the remainder of his working life. His services to Australia will become of more and more importance as research workers of the future make use of the material that he made available to them.

### BELGIUM

(From Our Regular Correspondent)

Oct. 8, 1938.

#### Benzenes, Benzines and Industrial Safety

Mr. A. Stassens has had published in *Industrie chimique belge* a noteworthy report on the medical aspect of the problem of benzenes ( $C_6H_6$ , or benzol), benzines (European industry calls the American "gasoline" also "benzine") and industrial safety; a discussion of all aspects, chemical, technical, professional, of the industrial use of hydrocarbons is included. Around 1936 a large number of serious cases of benzene poisoning were reported in various Belgian industries. Following these incidents, investigations were begun and Mr. Stassens collected a great deal of interesting information. The first part of the report is devoted to the benzene compounds (production, rectification, properties, utilization, methods of analysis). All relevant practical data with regard to the toxicity of these products is set forth. The second part of the report deals with the "benzines," substances which are still all too frequently confused with the benzene compounds. The author discusses the production of benzines, the refining process, the physical and chemical determinations used in analyses, the toxicity. All these points are the object of a detailed and careful study. In a third section of his report, Stassens discusses the problem of those closed chain compounds which, by their presence in essences of petroleum, impart formidable toxic properties to the latter. An appendix to the report contains the texts of all pertinent legislation. Physicians will read with interest this clear, complete and accurate portrayal of the contemporary question of hydrocarbons. They will simultaneously become convinced of the complex nature of the problem and of the need for active participation of doctors, as well as industrialists and workers, in the protection of that ever increasing number of persons in industry who are exposed to this particularly serious and fearful type of poisoning.

#### Yellow Fever in the Belgian Congo

Dr. Van Campenhout recently published a study on yellow fever in the Belgian Congo. A continuous and energetic crusade against *Aedes aegypti*, which is the main transmitting agent of the virus in epidemics in urban centers, is carried on. The sanitary conditions have been improved to such an extent in Matadi that the use of mosquito netting is no longer necessary. The examination of samples of liver tissues which were taken from cadavers in all suspected cases of yellow fever has not given, up till now, confirmation of the presence of the dis-

ease. Further examinations will be made on tissues taken from viscerotomy in new cases. Reports have been made on the communications recently passed to the International Office of Public Health. The head physician of the colony has not believed it his duty, up till now, to encourage the administration of anti-yellow fever vaccines although some volunteers asked to have them administered. There are many donors of immunizing serum. Disinfection of air ships in the Belgian Congo by the use of pyrethrum preparations has given satisfactory results. Fumigations are made just before embarkment and departure of the ship. The sanitary aerodromes of Leopoldville and Coquilhatville are provided with means against yellow fever. Elisabethville, Libenge and Boma aerodromes can be provided for this purpose in a few days if necessary.

### Professional Secrecy

An interesting discussion of professional secrecy was made by Dr. Heger in the Société de médecine légale of Belgium. The author called to mind a series of authoritative opinions with regard to the ethics to be maintained by physicians who also serve as officials of public or private organizations. He summarized his own views by saying that professional secrecy is unqualifiedly *de rigueur* for the practitioner who serves in an official capacity. The attending physician may furnish a certificate to a patient on request, but he is under no compulsion to do so. Dr. Ilivier asked the society's opinion on the following point: A medical expert is appointed by a court of law to ascertain the cause of death in an industrial accident case. For the fulfilment of his mission he must be in possession of all pertinent facts. Ought the attending physician to communicate his medical record of the accident victim to the medical examiner? Dr. Duvoir formally replied in the negative and cited a 1913 decision of the Court of Cassation, which holds that a criminal violation of medical secrecy has been committed as soon as the information has been divulged and regardless of the presence or absence of malicious intent. According to Dr. Duvoir the best procedure for a medicolegal expert to follow in general is this: The expert should advise the interested party to request of the injured person's physician a detailed certificate which the injured person could then submit to the expert. Dr. Daubrow objected that in the event of the patient's decease the claimants would have the status of third parties, and certificates delivered to third parties become *ipso facto* null and void. Under such circumstances an insurance company would be able to allege the incompetence of any certificate produced. Although a convinced upholder of professional secrecy, Dr. Daubrow could not help but admit that in certain cases the observance of secrecy may hamper the elucidation of the truth.

## Marriages

PAUL HARDIN HARMON to Miss Mary Logan Coleman, both of Springfield, Ill., September 13.

PAUL L. BERGSTROM, Kirkland, Ill., to Miss Lyne Gruhn of Columbus, Wis., September 4.

LIONEL GATES, Coalport, Pa., to Miss Mary H. Ryan of Mahanoy City, September 25.

HAROLD HENRI KLINGER, Akron, Ohio, to Miss Lucie Pickett of Fitzpatrick, Ala., recently.

MYRON REESE BAUMGARTNER to Miss Helen Berg, both of Dalton, Ohio, September 18.

WILLIAM T. DAILY, Brooklyn, to Miss Beatrix K. Robinson of New York, September 6.

HORACE F. BURTON, East Tawas, Mich., to Miss Helen Koth of Bay City, September 17.

ROBERT WILLIAM GRAVES to Miss Anne Yates, both of Durham, N. C., September 7.

REGINALD G. JOHNSTON to Mrs. Doris Greenwood, both of Medina, Ohio, recently.

## Deaths

**John Lawrence Yates** • Milwaukee; Johns Hopkins University School of Medicine, Baltimore, 1899; chairman of the Section on Surgery, General and Abdominal, American Medical Association, 1934-1935; assistant in pathology at his alma mater in 1901; assistant demonstrator of pathology at the University of Pennsylvania, Philadelphia, from 1902 to 1903; practiced in Milwaukee since 1906; member of the American Surgical Association, Society of Clinical Surgery and the American Association for Thoracic Surgery; fellow of the American College of Surgeons; served during the World War; consulting surgeon to the Milwaukee County and Milwaukee Children's hospitals, and attending surgeon to the Columbia Hospital; at one time on the staff of the Augustana Hospital, Chicago; aged 65; died, November 3, of a throat infection.

**Louis Marshall Warfield** • Milwaukee; Johns Hopkins University School of Medicine, Baltimore, 1901; member of the Association of American Physicians; fellow of the American College of Physicians; served during the World War; at one time associate professor of pathology, Milwaukee Medical College, professor of clinical medicine, Marquette University, instructor and lecturer on clinical chemistry and microscopy, Washington University Medical School, St. Louis, and professor of internal medicine at the University of Michigan Medical School, Ann Arbor; on the staffs of the Columbia, Evangelical Deaconess and Milwaukee County General hospitals; aged 62; was found dead in his automobile, September 28, of a bullet wound.

**John William Powers** • Milwaukee; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; clinical professor of orthopedic surgery, Marquette University School of Medicine; member of the Clinical Orthopedic Society and the American Academy of Orthopedic Surgeons; fellow of the American College of Surgeons; served during the World War; orthopedic surgeon to the Milwaukee County, St. Joseph's and Marquette University hospitals; aged 57; died, September 29, of arteriosclerosis.

**Adolf Gunderson** • La Crosse, Wis.; Koneglige Frederiks Universitet Medisinske Fakultet, Oslo, Norway, 1890; fellow of the American College of Surgeons; formerly member of the board of health; on the staffs of the La Crosse, Lutheran and St. Francis hospitals; at one time regent of the University of Wisconsin, Madison; aged 72; died, September 15, in Norway of bilateral nephrolithiasis, uremia and pyelonephritis.

**Harry Thomas Upshaw** • Pasadena, Calif.; St. Louis University School of Medicine, 1915; assistant clinical professor of surgery, University of Southern California School of Medicine, Los Angeles; fellow of the American College of Surgeons; on the staffs of the Huntington Memorial Hospital and the Los Angeles County Hospital; served during the World War; aged 46; died, August 12, of coronary thrombosis.

**Grafton Burke** • Fort Yukon, Alaska; University of the South Medical Department, Sewanee, Tenn., 1907; an Associate Fellow of the American Medical Association; fellow of the American College of Surgeons; for many years a medical missionary; medical director of the Hudson Stuck Hospital; aged 56; died, September 25, in the Virginia Mason Hospital, Seattle.

**Frank Wade Robertson**, New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1895; member of the American Psychiatric Association; at one time medical superintendent of Stamford (Conn.) Hall; formerly senior physician and superintendent of the Elmira (N. Y.) Reformatory; aged 69; died, August 27.

**William Howard Halsey**, San Diego, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; for many years a surgeon in the U. S. Navy; served during the World War; formerly on the staff of St. Mary's Hospital, Milwaukee; aged 54; died, August 14, of coronary thrombosis.

**Frank W. Hendley**, Cincinnati; Medical College of Ohio, Cincinnati, 1885; veteran of the Spanish-American and World wars; formerly medical officer and member of the claims board of the U. S. Veterans Bureau; medical director of the Cincinnati Mutual Life Insurance Company; aged 78; died, September 12, in the Christ Hospital.

**Alfred Careno Croftan** • Chicago; Hahnemann Medical College and Hospital, Chicago, 1896; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1898; at one time on the staff of St. Mary of Nazareth Hospital; aged 67; died, August 22, in Pasadena, Calif., of carcinoma of the colon.

**Robert Hollingsworth Potts** • New Orleans; Tulane University of Louisiana School of Medicine, New Orleans, 1918; assistant professor of medicine, Louisiana State University Medical Center; visiting physician to the Charity Hospital and on the staff of the Southern Baptist Hospital; aged 53; died, August 22.

**Argal Ernest Hubbard**, Oaklandon, Ind.; Chicago College of Medicine and Surgery, 1912; member of the Indiana State Medical Association; medical director and superintendent of the Sunnyside Sanatorium; formerly medical director of the Municipal Tuberculosis Sanitarium, Peoria, Ill.; aged 57; died, September 15.

**William Emmet Buehler** • Chicago; College of Medicine and Surgery, Chicago, 1904; Hering Medical College, Chicago, 1906; president emeritus and on the consulting staff of the Illinois Masonic Hospital; diagnostician on the staff of the American Hospital; aged 69; died, September 19, of coronary disease.

**William Townsend Dunning**, Gonzales, Texas; University of Texas School of Medicine, Galveston, 1909; member of the State Medical Association of Texas; served during the World War; formerly on the staff of the Holmes Hospital; aged 53; died, September 3, in the Nix Hospital, San Antonio.

**Pierson B. Peterson**, Honesdale, Pa.; Pulte Medical College, Cincinnati, 1891; member of the Medical Society of the State of Pennsylvania; formerly county coroner; at one time on the staff of the Wayne County Hospital; aged 74; died, August 8, of cerebral hemorrhage and arteriosclerosis.

**Mary Freyer Montgomery** • San Francisco; University of California Medical School, San Francisco, 1925; assistant clinical professor of surgery at her alma mater; assistant attending staff member, Children's Hospital; aged 39; died, August 30, in the University of California Hospital.

**Thomas Micajah Fly** • Little Rock, Ark.; University of Arkansas School of Medicine, Little Rock, 1903; formerly on the faculty of the University of Arkansas School of Medicine as associate in medicine; city health officer; aged 58; was found dead, September 21, of coronary occlusion.

**Leslie Ramsey Hazlett** • Butler, Pa.; Jefferson Medical College of Philadelphia, 1896; member of the American Academy of Ophthalmology and Oto-Laryngology; on the staff of the Butler County Memorial Hospital; aged 70; died, August 10, of coronary occlusion.

**Jonas Zettlemoyer**, Philadelphia; Temple University School of Medicine, Philadelphia, 1914; member of the Medical Society of the State of Pennsylvania; for many years connected with the bureau of public health; aged 75; died, August 9, in the Presbyterian Hospital.

**George F. Weber**, Ira, N. Y.; College of Physicians and Surgeons, Baltimore, 1889; at one time county coroner; for many years health officer; aged 74; died, August 30, in the Syracuse (N. Y.) Memorial Hospital of coronary thrombosis and diabetes mellitus.

**Otto Frederick Aufderheide**, St. Louis; Homeopathic Medical College of Missouri, St. Louis, 1900; member of the Missouri State Medical Association; aged 60; died, September 14, in the Christian Hospital, of intestinal obstruction due to intussusception.

**William Curtis Cross**, Ashtabula, Ohio; Cleveland University of Medicine and Surgery, 1896; veteran of the Spanish-American War; at one time member of the city board of education; aged 65; was killed, September 7, in an automobile accident.

**Frank Louis Waite** • Hartford, Conn.; Bellevue Hospital Medical College, New York, 1888; member of the American Ophthalmological Society; aged 72; on the staff of the Hartford Hospital, where he died, August 31, of cerebral thrombosis.

**Hugo Alexander**, Hoboken, N. J.; Columbia University College of Physicians and Surgeons, New York, 1911; member of the Medical Society of New Jersey; served during the World War; aged 51; died, September 14, of coronary embolism.

**Chester Arthur Miller**, Thedford, Neb.; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1902; served during the World War; aged 64; died, August 29, in the Mercy Hospital, Council Bluffs, Iowa, of leukemia.

**Victor Bychower**, Malden, Mass.; Kaiser-Wilhelm-Universität Medizinische Fakultät, Strassburg, Germany, 1888; member of the Massachusetts Medical Society; aged 77; died in September at Bethlehem, N. H., of cerebral hemorrhage.

**Giles Edward Harris**, Hugo, Okla.; Louisville (Ky.) Medical College, 1905; member of the Oklahoma State Medical Association; served during the World War; aged 60; died in September of injuries received in an automobile accident.

**Luther Clarence Neill**, George Washington University School of Medicine, 1904; veteran of the Spanish-American War; aged 61; died, August 10, of rupture of aneurysm of the aorta and arteriosclerosis.

**Carl Schumann**, Delhi, N. Y.; New York Homeopathic Medical College and Hospital, 1887; member of the Medical Society of the State of New York; aged 75; died, August 2, in the Delhi Hospital of arteriosclerotic heart disease.

**Augustus Camillus Connor** Ⓢ Lexington, Texas; University of Louisiana Medical Department, New Orleans, 1883; past president of the Lee County Medical Society; aged 79; died, September 1, of hypostatic pneumonia.

**Charles Highsmith**, Dunn, N. C.; Baltimore Medical College, 1898; member of the Medical Society of the State of North Carolina; aged 66; died, September 9, in the Highsmith Hospital, Fayetteville, N. C., of pneumonia.

**Theodore Edward Schwarz**, Oakland, Calif.; Medical College of Ohio, Cincinnati, 1900, 1885; member of the California Medical Association; served during the World War; aged 60; died, August 4, of coronary thrombosis.

**Gustavus Crocker Simmons** Ⓢ Inverness, Calif.; Harvard University Medical School, Boston, 1885; at one time mayor of Sacramento and president of the board of health; aged 75; died, August 8, of coronary occlusion.

**Edward Everett Barbour**, Peoria, Ill.; Physio-Medical College of Indiana, Indianapolis, 1899; member of the Illinois State Medical Society; aged 69; died, September 22, of lobar pneumonia and Parkinson's disease.

**Rose D. Howe Jameson**, Bethlehem, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1891; member of the Connecticut State Medical Society; aged 73; died, August 17, of cerebral thrombosis.

**True Deloss Coe** Ⓢ Keithsburg, Ill.; Rush Medical College, Chicago, 1884; past president of the Mercer County Medical Society; aged 78; died, September 7, in a hospital at Monmouth of pneumonia.

**Kenneth Franklin Hughes**, St. Louis; University of Illinois College of Medicine, Chicago, 1937; aged 29; was killed, September 15, when the automobile in which he was driving was struck by a train.

**John G. W. Knoll**, Buffalo; University of Pennsylvania Department of Medicine, Philadelphia, 1888; for many years on the staff of the Deaconess Hospital; aged 73; died, August 26, of food poisoning.

**Anthony Caputi**, Brooklyn; Hahnemann Medical College and Hospital of Philadelphia, 1935; aged 30; on the staff of the Prospect Heights Hospital, where he died, September 5, of pneumonia.

**Edward Freeman Walsh**, Pasadena, Calif.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1886; aged 80; died, August 31, of diabetes mellitus.

**Alberto Garcia de Quevedo**, Washington, D. C.; University of Maryland School of Medicine, Baltimore, 1915; aged 45; died, August 29, of cirrhosis of the liver and diabetes mellitus.

**James Ignatius Keaney Jr.**; St. Joseph, Mo.; St. Louis University School of Medicine, 1906; on the staff of the State Hospital Number 2; aged 62; died, September 9, of cardiac disease.

**Harry Samuel Hughes** Ⓢ St. Louis; St. Louis University School of Medicine, 1905; aged 56; was killed, September 15, when the automobile in which he was driving was struck by a train.

**William F. Berkenstock**, Philadelphia; Hahnemann Medical College of Philadelphia, 1884; aged 76; died, September 5, in Atlantic City, N. J., of arteriosclerosis and aortic stenosis.

**William Frederick Imrie Dey**, New York; University of Toronto Faculty of Medicine, 1910; served during the World War; aged 56; died, September 16, of heart disease.

**Clarence S. Branson** Ⓢ St. Joseph, Mo.; Ensworth Medical College, St. Joseph, 1910; on the staff of St. Joseph's Hospital; aged 50; died, September 16, of coronary thrombosis.

**William Herbert Nute** Ⓢ Exeter, N. H.; Medical School of Maine, Portland, 1881; on the staff of the Exeter Hospital; aged 80; died, August 18, of coronary thrombosis.

**Thomas Bassett Keyes** Ⓢ Lake Bluff, Ill.; Albany (N. Y.) Medical College, 1895; aged 62; died, October 2, of myocarditis.

**Andrew Foster Whitford**, Cambridge, Mass.; Baltimore University School of Medicine, 1893; died, August 24.

## Correspondence

### MEETING OF THE AMERICAN PUBLIC HEALTH ASSOCIATION

*To the Editor:*—I have just read the interesting editorial on page 1770 of THE JOURNAL of November 5 and also the news item on page 1775 with regard to the action of the American Public Health Association at its sixty-eighth annual meeting at Kansas City, Mo., October 25-28. Every one in attendance at the meeting was very much distressed at the total misconception of the attitude and action of the association by the public press, but we are much more disturbed because of the failure by THE JOURNAL to understand this action. The resolutions speak for themselves. The following resolution was written by Dr. Abel Wolman, the distinguished sanitary engineer of Baltimore, who is president of the association, and was unanimously adopted on motion of Dr. Thomas Parran, Surgeon General of the U. S. Public Health Service:

The American Public Health Association records its appreciation of the participation in its deliberations during this annual meeting week of Dr. Irvin Abell, President of the American Medical Association. It records with pleasure its agreement with the approval in principle, at a recent special session of the House of Delegates of the American Medical Association, of the content of the National Health program presented by the Interdepartmental Committee to the National Health Conference. The association pledges its continued cooperation and support to the American Medical Association in the translation of this policy into action.

There was no difference of opinion expressed in the Governing Council, which corresponds with the House of Delegates of the American Medical Association; the resolution with regard to the Report of the Technical Committee on Medical Care as published in THE JOURNAL expressed exactly the unanimous feeling of the Governing Council. There was not a single expression made in favor of so-called health insurance and there was no difference of opinion between the medical and lay members of the association. The action was unanimous, the consideration was as constructive and on as high a plane as that of the memorable special session of the American Medical Association in Chicago, and the practical agreement between the American Medical Association and the American Public Health Association should be emphasized, rather than the studied effort to create the impression that there was a division of opinion.

I am sorry that you and every other thoughtful member of the medical profession could not have been present at this meeting, where those who specialized in public health found themselves in practically complete accord with the splendid statement made by Dr. Irvin Abell as President of the American Medical Association.

Following the adoption of the resolution, and the precedent set by the American Medical Association, the following committee was appointed to confer with the Interdepartmental Committee, the American Medical Association, the American Dental Association, the National Organization of Public Health Nurses, the Conference of State and Territorial Health Officers and other agencies: Drs. Abel Wolman, president of the association, as chairman; J. N. Baker of Alabama; Louis I. Dublin, vice president of the Metropolitan Life Insurance Company of New York; Harry S. Mustard of New York; John L. Rice of New York; Felix J. Underwood of Mississippi, and myself. Drs. E. S. Godfrey, president-elect, and Reginald M. Atwater, executive secretary of the association, are ex officio members.

As you know, Dr. Baker, Dr. Underwood and I are members of the House of Delegates of the American Medical Association. The chairman of the Committee on Resolutions was Dr. A. J. Chesley of Minnesota, who is secretary of the Conference of State and Territorial Health Officers and a member of the Committee on Study of Medical Care of the American Medical Association.

I desire respectfully to submit that those of us interested in the preservation of the integrity and traditions of American

medicine can serve it and the American people better by emphasizing the essential unity of all branches of the medical and allied professions in support of the constructive sections of the National Health Program, and in the practically unanimous objection to compulsory health insurance, than by reemphasizing the captious objections raised by individuals in the various organizations.

A. T. McCORMACK, M.D., Louisville, Ky.

## Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

### DIVERTICULITIS

*To the Editor:*—A patient aged 55 has had vague abdominal pains for nearly a year. Most of the pain seems to be in the left lower quadrant. Complete examination is quite normal except for a blood pressure of 166 systolic, 104 diastolic and extreme nervousness. X-ray examination of the stomach, gallbladder and lungs is normal; the electrocardiogram is normal. A barium sulfate enema reveals diverticula in the sigmoid with rather marked spasm at the junction of the descending and sigmoid colon. I have tried many diets and various medications, such as atropine, phenobarbital and bromides. The bowels are not constipated. I would appreciate anything further you may suggest.

M.D., Ohio.

**ANSWER.**—The abdominal distress is undoubtedly due to the diverticula and associated local spasm. Because of the patient's hyperkinetic state he is more susceptible to pain stimuli. The treatment should consist of a nonresidue diet and an oil retention enema each night of 3 or 4 ounces (about 100 cc.) of olive oil, to which 20 grains (1.3 Gm.) of thymol iodide powder should be added. Antispasmodics should be tried such as novatropine. If these measures fail, an attempt may be made to fill the diverticula with a nontoxic substance. This can be accomplished by giving barium sulfate or bismuth subcarbonate in 2 ounce (60 Gm.) doses once a week for six weeks.

### SKIN GRAFT TO FINGER TIP

*To the Editor:*—When a patient accidentally cuts off the end of the finger tips for from one-fourth to one-half inch, leaving the bone exposed, would it be feasible to use a plaster cast immobilizing the hand and arm to the opposite side of the patient's abdomen and making a graft of the skin from that area to cover the stumps? Will such skin later provide a serviceable practical skin that will stand up satisfactorily under hard physical usage?

M.D., California.

**ANSWER.**—The immediate covering of such losses, where the wound has been from a clean cut rather than a crushing one, is desirable and the skin of the flank is acceptable. Occasionally, by simply flexing the finger on the hand, a small flap from the hand can be put in place. Still more infrequently it may be possible, if there has been a clean excision of the tip of a finger, to do a free graft provided the tip itself has not been too greatly contaminated. The transplanted skin from any area will not have the characteristic tough padding of the finger tip and may need the protection of a glove if exceptionally hard work is to be done.

### ARTHRANOL, ERTRON AND LYXANTHINE-ASTIER

*To the Editor:*—What information can you give me concerning the following in the treatment of arthritis? (1) Arthranol (*Time*, Sept. 26, 1938); (2) Ertron (Nutrition Research Laboratories, Inc., Chicago); (3) Lyxanthine-Astier (Gallia Laboratories, Inc., New York).

M.D., Brockport, N. Y.

**ANSWER.**—1. Arthranol, stated to be a mixture containing essentially ammonium phosphate, ammonium iodide, ammonium chloride, ammonium benzoate, ammonium salicylate and water, was discussed editorially in *THE JOURNAL* October 8, page 1381. It is recommended for use in the treatment of arthritis, but no competent evidence is available to indicate its usefulness.

2. Ertron was the subject of an adverse report of the Council on Pharmacy and Chemistry (*THE JOURNAL*, July 10, 1937, pp. 132 and 133). It is claimed to be a highly potent vitamin D preparation. The Council found no evidence to establish the value of such preparations in the treatment of arthritis.

3. Lyxanthine-Astier has not been examined by the Council nor has the American distributor, Gallia Laboratories, Inc.,

requested the Council to consider the preparation for the purpose of determining its eligibility for inclusion in New and Nonofficial Remedies.

According to advertising material distributed by the Gallia laboratories in 1936, Lyxanthine-Astier is a "new product developed by the famous research laboratories of Dr. P. Astier of Paris, France," an "efficient anti-arthritis, antirheumatic" associating "sulphur, calcium and iodine with the potent uric acid solvent, lysidin bitartrate." The following formula appears in the advertising: "Iodo-propanol-sulphonate of sodium 12 grs., bitartrate of lysidin 9 grs., calcium gluconate 12 grs., sodium bicarbonate 37 grs., tartaric acid 15 grs., citric acid 6 grs., powdered sugar 9 grs., oil of lemon, several drops."

Although lysidin is claimed to be the "main active element" of Lyxanthine, in his studies carried out some twenty years ago, Hanzlik reached the conclusion that there is sufficient scientific evidence to indicate the worthlessness of lysidin as a urate solvent (*J. Lab. & Clin. Med.*, February 1917; Report of the Therapeutic Research Committee, 1917). The other active "anti-rheumatic agents" of Lyxanthine are stated to be iodine and sulfur in the form of iodo-propanol sodium sulfonate and calcium gluconate. The latter substance has been accepted by the Council for inclusion in New and Nonofficial Remedies as the effective agent for obtaining the therapeutic effects of calcium. However, the Council's publication gives no recognition to claims of usefulness as a treatment for arthritis.

Lyxanthine-Astier appears to be a needlessly complex and unscientific mixture of well known substances marketed under a fanciful name with claims that have not been confirmed by competent investigations.

### BILATERAL PHRENICECTOMY FOR TUBERCULOSIS

*To the Editor:*—Is bilateral permanent phrenicectomy compatible with life where the operations on the two sides are done at long intervals on persons who have adequate functional lung tissue in the upper portions?

M.D., California.

**ANSWER.**—Not only is bilateral phrenicectomy compatible with life but even simultaneous bilateral phrenic exeresis may be performed without causing visible harm. In dogs, unilateral multiple intercostal nerve paralysis has been performed, in addition, without causing death. W. S. Lemon (*Am. J. M. Sc.* 177:319 [March] 1929) reported one dog on which he did complete bilateral, intercostal neurectomy and bilateral phrenic paralysis in four stages without death, and without dyspnea except under anesthesia. The advisability of such operations is another matter. Alexander (Collapse Theory of Pulmonary Tuberculosis, 1937, p. 152) says that he has never seen a patient for whom a permanent bilateral phrenic paralysis was indicated. Even temporary bilateral paralysis is rarely performed. Alternating temporary paralysis, however, is not infrequently resorted to, time being allowed for function to return to the side operated on first.

### HEMOPHILIA

*To the Editor:*—A boy aged 16 is a real hemophiliac. Recently I read in the *Lancet* (2:1142-1149 [Nov. 14] 1936, about a supposed aid in hemophilia. The article spoke of mixing egg white with potassium bromide and keeping this mixture in an incubator at body temperature for several days. Then this mixture was injected for treatment of the blood condition. Is there any scientific basis for this mixture doing any good?

J. H. BURROWS, M.D., Williamsport, Pa.

**ANSWER.**—Recent research in hemophilia has been directed toward a study of the blood serum. The investigations of Patek and Taylor (*J. Clin. Investigation* 16:133 [Jan.] 1937) and of Pohle and Taylor (*ibid.* 16:741 [Sept.] 1937) have suggested that in hemophilia there may be a deficiency in certain serum globulins. They have shown that a globulin substance prepared from normal human serum accelerates clot formation of hemophilic and normal blood but that hemophilic blood serum lacked this property. A similar theory is suggested by the studies of Eley, Green and McKhann (*J. Pediat.* 8:135 [Feb.] 1936) and of Bendien and Grevel (*Acta. brev. Neerland.* 5:135, 1936) on the effects in hemophilic patients of human placental extract, which may contain a similar globulin substance.

There may be some relation between these studies and those of Timperley, Naish and Clark referred to in the question. These authors report that repeated injection of an extract prepared from egg white reduces the clotting time and controls hemorrhage in hemophilic patients. The apparently favorable results reported by them have not as yet been corroborated by others. No further reports on the use of this preparation have appeared in the American or European literature. As the authors themselves state, more study and prolonged testing is necessary before an evaluation of the effect of this substance can be made.

## TREATMENT OF SYPHILIS

To the Editor:—A woman aged 27, separated from her husband, came to me June 6, 1936, for a check up at the insistence of a partner who had contracted a virulent case of gonorrhea. She stated that she had never had a venereal infection or any symptoms relative to the genital tract and he emphatically denied any other source of contact. Another physician had previously taken urethral, vaginal and cervical smears and had found them negative. I repeated the smears and also took blood for a Hinton and a complement fixation test. The smears came back negative but the blood reports were positive for both syphilis and gonorrhea. I repeated the test and got the same results. Since then the woman has been under my care and has had the following medication with the following results: one course of nearsphenamine totaling thirteen injections or 5.95 Gm. The Hinton test after the seventh injection gave positive results. One course of twelve thiobismol injections totaling 34.4 Gm. The Hinton test after the eighth injection was positive and the spinal fluid reading of the colloidal gold test was 00+1100000. The Wassermann reaction of the spinal fluid was negative. Because of reactions with nearsphenamine I tried starting the second course of arsenicals with mapharsen and gave two injections of 0.04 Gm. each. On the third injection I reverted to nearsphenamine, giving 0.3 Gm. Twelve more injections of sulfarsphenamine were then given, totaling 3.9 Gm. The substitution was made because of difficulty with small veins. The Hinton reaction after the sixth and fifteenth treatments was still positive. After the fifteenth treatment the complement fixation test was positive. The spinal fluid examination gave a negative Wassermann reaction and colloidal gold ++++000. The second bismuth course consisted of five injections of thiobismol (15 grains) and five injections of bismuth subsalicylate in oil (14 grains). There have been seven injections of sulfarsphenamine in the third course, totaling 2.1 Gm. The Hinton reaction following the last injection was still positive. To date the patient has had nearsphenamine 6.25 Gm., sulfarsphenamine 6 Gm., mapharsen 0.08 Gm., thiobismol 49.4 grains, bismuth subsalicylate 14 grains. In conjunction she has also had two courses of yellow mercurous iodide one-eighth grain (0.008 Gm.) three times a day for one month each. She has been lax in receiving treatment and should have had nearly double this amount had she been regular. In addition she married again one year ago without permission and has since had two miscarriages at the third month. I had planned to give eight more injections of sulfarsphenamine and ten more of bismuth subsalicylate in oil before allowing a period of probation. What chance is there to develop central nervous system syphilis and what should be done to prevent it as much as possible? Is there any likelihood of infecting her husband? Will it be possible to reverse the Hinton reaction at this late date and what should be done to favor it? Would tryparsamide be indicated? Will it be possible for her to carry to term successfully?

M.D., Massachusetts.

ANSWER.—This patient has received fourteen injections of nearsphenamine totaling 6.25 Gm., nineteen injections of sulfarsphenamine totaling 6 Gm., two injections of mapharsen totaling 80 mg., seventeen injections of thiobismol totaling 1.27 Gm. of metallic bismuth, and five injections of bismuth subsalicylate totaling 0.325 Gm. of metallic bismuth.

Some of the other data that are most necessary, however, are not furnished. No mention is made of physical examination—simply laboratory data are furnished. No mention is made of anything in the spinal fluid but the colloidal gold test and the Wassermann reaction. In an early lumbar puncture the cell count is most valuable. Moreover, it is not stated how often thiobismol injections were given. This may be one of the reasons why the patient has not responded better to therapy, though it is true that she apparently has been negligent. Studies by Sollmann, Cole and Henderson (*Ann. J. Syph.*, 21:480 [Sept.] 1937) have shown that thiobismol must be administered three times a week to achieve a therapeutic lasting level of bismuth in the blood stream. If the injections are given but once a week there is little or no effect on the syphilis, for the peak level of bismuth in the blood stream after a single injection is reached and is over in twenty-four hours, and thereafter there is only a small level, which continues for a few days. On that account, if one uses thiobismol the injections must be given three times a week.

It would be well to go over the patient carefully, looking particularly for evidence of cardiovascular syphilis and for central nervous system involvement. Moreover, a lumbar puncture should be done at once, a cell count, a colloidal gold test, a Pandy test, and a Wassermann test on the fluid in amounts of 0.1 cc. up to 1 cc.

It is possible that the patient has had her syphilis for some time, and if this is true there would not be so much danger of her husband's being infected. He should be examined, however, and a Wassermann test taken.

If the lumbar puncture is done now and is negative, and the physical examination shows no evidence of central nervous system involvement, the chances are that the patient will not develop central nervous system involvement after this period of time. The Cooperative Clinical Group studies have shown that practically all involvement of the central nervous system actually occurs early in the infection although symptoms may not appear for years. Tryparsamide would not be indicated unless there is involvement of the central nervous system.

If physical examination is negative and if the lumbar puncture is entirely negative, this patient should receive alternating courses in a continuous manner of ten injections each of nearsphenamine or mapharsen and of bismuth subsalicylate for a further period of one year and in the succeeding year two courses of injections of bismuth subsalicylate with a rest period between the courses. The Cooperative Clinical Group has already recommended that every syphilitic woman who is pregnant should be treated for syphilis throughout the pregnancy. This gives the best promise of a living, healthy child.

## TULAREMIA

To the Editor:—A patient died from an infection at first presumed to have been caused by cigaret ashes which flew into his right eye. He rubbed the eye and it was red and irritated and later became infected. At first it was diagnosed as streptococcal infection but it did not respond to treatment. Blood tests were made, the first two being negative for tularemia. It had been suggested that there was a tularemic ulcer under the upper lid of the right eye. Further tests showed tularemia and treatment was given but the patient developed pneumonia and died. Autopsy disclosed the tularemia germ. As I understand it there are only about fifty cases reported of the ocular glandular type of tularemia. Could it be possible for this patient to have been bitten by a tick and for the poison to have gone through his system and settled in his eye? Is it possible for the tularemia germ to enter through the pores of the skin without the avenue of an abrasion or opening to the blood stream? A theory has been advanced that he might have smashed a tick with his fingers, wiped it on his trousers or clothes and later came in contact with it by his hands and rubbed it into his eye. The man was a fastidious individual, meticulous in his habits, and immediately preceding the episode when he got the ashes in his eye he had bathed thoroughly and had not handled any rabbits or been in contact with any. He had been out to a dude ranch the day this happened but stated that he was not bitten by a tick. Nor was he where he would come in contact with ticks other than being in the early morning outside the main ranch building with a lariat that belonged to him, throwing it to lasso a post. But after that he swam in the pool and bathed several times. His first complaint of his eye was when he and a young woman were riding home, both smoking cigaretts, and a gust of wind blew the ashes into the eyes of both. The woman was not affected at all, but the patient rubbed his eye rather violently and later stopped and bathed it with water.

ROBERT R. HARROLD, North Hollywood, Calif.

ANSWER.—The presence of an ulcer from tularemia under the upper eyelid of the right eye leaves little doubt that this ulcer was the primary lesion and that the invasion of other tissues was secondary to the eye infection.

There seems to be unmistakable evidence that the causative organism of tularemia may invade unbroken skin or mucous membrane. In glandular tularemia there is no demonstrable primary ulcer. It is possible to infect guinea pigs and rabbits by dropping a suspension of infected tissue of the spleen onto the skin or into the conjunctival sac.

The development of oculoglandular tularemia usually results from inadvertently wiping the eye with fingers that have been contaminated by handling infected animals or by crushing an infected wood tick or deer fly.

## ALOPECIA FROM LUPUS ERYTHEMATOSUS

To the Editor:—Since the age of 6 an unmarried woman aged 21 has had alopecia in the frontal and occipital regions of the scalp as a consequence of a probable lupus erythematosus. The few scattered hairs in the scarred regions are fine and short; the marginal hairs are longer and thicker. Hence she has had to wear a wig. What procedure besides scalp grafting is possible? Can individual hairs be sewed into the scalp? What is the relative efficacy of the different methods? Any treatment even of doubtful merit will be carefully considered. M.D., New York.

ANSWER.—Unfortunately lupus erythematosus when it affects the scalp produces areas of alopecia and atrophy. The only recourse this patient can have is wearing a wig. Grafting hair on the scalp and sewing hairs into the scalp are impossible procedures.

## SYMPATHECTOMY FOR SPASTIC PARALYSIS

To the Editor:—I would appreciate information as to the merit of sympathectomy for an after-birth hemiplegic spastic paralysis due to cerebral hemorrhage.

M.D., New York.

ANSWER.—The enthusiasm created by the work of Hunter and Royle during their visit to the United States in 1924, when they proposed the operation of sympathectomy for the purpose of relieving spasticity in cerebrospastic paralysis, has long since subsided. Patients who appeared to be benefited shortly after operation were found within a short time to be as spastic as they had been previous to the operation. From the standpoint of clinical experience in the use of this operative procedure, it is doubtful whether there is any permanent benefit to be derived from it.

## POWDERS FOR ALCOHOLISM

To the Editor:—1. There has come to my attention recently a powder which is used to place in alcoholic beverages and causes immediate sickness; it is said to terminate the effects of overindulgence of alcohol immediately. This I cannot believe. The names of the two powders mentioned are "Micky Finn" and "Mrs. Moffat's Shoo Fly Powder." Can you give me some information on this subject? 2. Is there any powder which can be added to an alcoholic beverage that cannot be detected by taste and will cause a distaste to alcohol? M.D., Massachusetts.

ANSWER.—1. The report on the Mickey Finn Powders was sent to the American Medical Association Chemical Laboratory Nov. 22, 1918, by Dr. William D. McNally, then coroner's chemist for Cook County. The product was labeled "Mickey Finn Powders—Great Antidote for the Liquor Habit." The powder weighed from 9.57 to 13.56 grains and contained 98.19 per cent tartar emetic. Similar analysis of "Mrs. Moffat's Shoo Fly Powders" showed that each powder weighed from 2.88 to 2.97 grains. An analysis showed 98.6 per cent tartar emetic.

2. No.

## POSSIBLE GLOMUS TUMOR

To the Editor:—A patient has numerous subcutaneous nodules, some about the size of a pea, some about half that size. They are painful. One of them has been removed and examined by a competent pathologist, who diagnosed it as angiofibroma. He had no treatment to offer. The patient is suffering severely and so far the only thing that I have found to give her relief has been salicylates. However, she is having as much trouble now as she had eight months ago, and I wonder whether there is any therapy that will cure this condition.

A. C. FORTNEY, M.D., Fargo, N. D.

ANSWER.—From the meager description of a painful tumor of the skin, the deduction is that this patient most probably has a glomus tumor. One might suggest a recheck of the case and comparison of the pathologic slide with the published accounts of the microscopic appearance and the clinical picture of glomus tumor. (Andrews, G. C.: Textbook of Dermatology, ed. 2, Philadelphia, W. B. Saunders Company, 1938, p. 705). Treatment consists of removing each nodule surgically. Electro-surgery also may be used.

## COMPRESSES IN CELLULITIS

To the Editor:—THE JOURNAL, September 3, page 960, carries an answer to the question What is the rationale of cold compresses of magnesium sulfate in cellulitis? I would like to call your attention to the answer, which states that "hot wet dressings produce an edema of the underlying tissue and capillary changes in the vessels with a varying amount of cellular infiltration." This answer is at variance with factual information in the field of capillary physiology. Local edema due to a cellulitis does not develop if circulation is maintained. Moist heat induces local circulatory acceleration. During work muscles take up from ten to twenty times more oxygen than when at rest. Heat, within certain limits, influences oxygen diffusion about 1 per cent per degree. This indicates increased capillary circulation in order to supply the oxygen. If the circulation was not accelerated by moist heat and by functional activity, the rapid exhaustion of oxygen from the blood would result in a cyanotic color which is characteristic of poor circulation. One does not see cyanosis from the use of moist heat compresses. Carbonic acid is inseparably bound up with increased functional activity. Pure carbon dioxide will produce dilatation of arteries and capillaries and a rapid current of blood. There is no reason for believing that the accelerated circulation induced by moist heat can be produced independently of the formation of carbon dioxide. Clinically, the picture induced by muscular activity and the picture induced by moist heat are similar. Krogh (The Anatomy and Physiology of Capillaries, New Haven, Conn. Yale University Press, 1929) found when working with rabbits that if the animals were kept warm the arteries and arterioles were dilated; the capillaries were not greatly involved in the dilatation but the venules and veins were somewhat dilated by the increased flow. In the skin of man, moderate moist heat does not induce the contracted, elevated papillae of refrigeration. It must be remembered that there are no capillaries in the skin of man outside those in the papillae. In a study of capillary loops around the finger tips of man, Krogh noted that warmth allowed two corpuscles to pass the field of vision when normally only one had been noted. Under the influence of cold, agglutination of corpuscles was noted and the flow appeared retarded. Clinically, if vessels are not damaged and the circulation has not failed completely, local edema disappears under moist heat compresses. Naturally there is a limit to physiologic reactions. If capillary function has failed completely, surgery is indicated, not therapy. "Changes" in capillary walls and cellular infiltration are not the result of application of compresses of moist heat. If uncontrolled dry heat or refrigeration is used, "changes" may be expected. A better understanding of the physiology of capillary function should result in the abandonment of cold packs as a means of combating a localized suppurative cellulitis. Dental and mastoid suppurations are commonly refrigerated. The abdomen is commonly refrigerated with ice packs. Enough evidence is available today to indicate that refrigeration of a local cellulitis is empiricism.

JOSEF NOVITZKY, D.D.S., San Francisco.

## Medical Examinations and Licensure

## COMING EXAMINATIONS

## STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, November 12, page 1871.

## NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Medical centers having five or more candidates desiring to take the examination, Feb. 13-15. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th Street, Philadelphia.

## SPECIAL BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: An Affiliate of the American Board of Surgery. Written examination, Part I, will be held in various cities of the United States and Canada, April 8. Oral examinations for all candidates, St. Louis, May 13-14. Applications must be filed not later than sixty days prior to the date of the examinations. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF INTERNAL MEDICINE: Written examinations will be held in various parts of the United States, Feb. 20. Application must be received on or before Jan. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Written examination and review of case histories of Group B applicants will be held in various cities of the United States and Canada, Feb. 4. General oral, clinical and pathological examinations for all candidates (Groups A and B) will be given in St. Louis, May 15-16. Applications must be filed not later than sixty days prior to the date of examination. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: St. Louis, May 15. Applications must be filed before February 15. Sec., Dr. John Green, 3720 Washington Blvd., St. Louis.

AMERICAN BOARD OF ORTHOPEDIC SURGERY: Memphis, Tenn., Jan. 13-14. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: St. Louis, May 12-13. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PEDIATRICS: New York, April 26. Appointments must be made before Dec. 26. St. Louis, May 16. Appointments must be made before Jan. 16. Cincinnati, Nov. 14-15. Appointments must be made before July 14. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 28-30. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: St. Louis, May 11-14. Sec., Dr. Byrl R. Kirklind, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: New York, Jan. 13-15. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

## Missouri June Report

Dr. Harry F. Parker, secretary, State Board of Health of Missouri, reports the written examination held at St. Louis, June 2-4, 1938. The examination covered fifteen subjects. An average of 75 per cent was required to pass. One hundred and sixty-five candidates were examined, 162 of whom passed and three failed. Fifteen physicians were licensed by reciprocity and five physicians were licensed by endorsement July 26. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
State University of Iowa College of Medicine.....	(1937)		79.5
University of Kansas School of Medicine.....	(1933)		81.7
Johns Hopkins University School of Medicine.....	(1932)		85.3
Harvard University Medical School.....	(1937)		82.6
St. Louis University School of Medicine.....	(1937)		76.8
76.8, 79, 80.4, 81.4, 81.8, 82.4, (1938) 76.9, 77.5, 78, 78.1, 78.4, 78.4, 78.9, 79, 79.4, 79.9, 80, 80, 80.1, 80.1, 80.2, 80.4, 80.5, 80.5, 80.6, 80.7, 80.8, 81.1, 81.2, 81.3, 81.4, 81.4, 81.5, 81.6, 81.8, 81.8, 81.9, 82, 82, 82.1, 82.2, 82.2, 82.3, 82.4, 82.4, 82.5, 82.5, 82.7, 82.8, 83.4, 83.4, 83.8, 84.1, 84.1, 84.6, 84.7, 84.8, 84.8, 85.2, 85.2, 85.4, 85.6, 86.3, 87, 87.5, 88.4, 88.7, 89.6			
Washington University School of Medicine.....	(1937)		75.2
75.4, 77.7, 77.8, 81.1, (1938) 76.5, 77.2, 78, 78, 78.6, 79.2, 79.3, 79.5, 79.5, 79.6, 79.7, 79.8, 80, 80, 80.1, 80.4, 80.5, 80.6, 80.6, 80.6, 80.6, 81, 81.1, 81.2, 81.3, 81.3, 81.4, 81.4, 81.4, 81.5, 81.6, 81.6, 81.6, 81.6, 81.7, 81.7, 81.8, 81.8, 82, 82.1, 82.1, 82.2, 82.2, 82.5, 82.5, 82.6, 82.6, 82.8, 82.8, 82.8, 82.9, 83, 83.1, 83.2, 83.3, 83.4, 83.6, 83.6, 83.8, 84.1, 84.1, 84.2, 84.4, 84.4, 84.6, 84.6, 84.6, 84.6, 84.8, 85, 85.2, 86, 86.4, 86.4, 87.3			
Creighton University School of Medicine.....	(1936)		80
University of Nebraska College of Medicine.....	(1937)		83.1
University of Pennsylvania School of Medicine.....	(1937)		81.1
Baylor University College of Medicine.....	(1937)		85.7
University of Texas School of Medicine.....	(1937)		80.4
University of Wisconsin Medical School.....	(1937)		77.4, 78.8
McGill University Faculty of Medicine.....	(1923)		82.7
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin.....	(1937)		76.8
School	FAILED	Year Grad.	Per Cent
School of Medicine of the Division of Biological Sciences.....	(1937)		74.2
Meharry Medical College.....	(1935)	69.6, (1937)	72.7
School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Arkansas School of Medicine.....	(1937)		Arkansas
University of Colorado School of Medicine.....	(1936)		Colorado
Emory University School of Medicine.....	(1937)		Georgia



University of Kansas School of Medicine.....(1931), (1935), (1937, 3) Kansas	
University of Louisville School of Medicine..(1934), (1937)	Kentucky
Tulane University of Louisiana Medical Department..(1912)	Louisiana
Johns Hopkins University School of Medicine.....(1935)	Maryland
Harvard University Medical School.....(1936)	Maine
Creighton University School of Medicine.....(1936)	Kansas
Meharry Medical College.....(1934)	Tennessee
School	LICENSED BY ENDORSEMENT
College of Medical Evangelists.....(1937) N. B. M. Ex.	Year Endorsement
Tulane University of Louisiana School of Medicine..(1936) N. B. M. Ex.	Grad. of
St. Louis University School of Medicine.....(1931) N. B. M. Ex.	
Washington University School of Medicine.....(1936) N. B. M. Ex.	
Cornell University Medical College.....(1935) N. B. M. Ex.	

## Book Notices

**The Biology of Arteriosclerosis.** By M. C. Winternitz, M.D., R. M. Thomas, M.D., and P. M. LeCompte, M.D., the Department of Pathology, Yale University School of Medicine, New Haven, Connecticut. Cloth. Price, \$4. Pp. 142, with 116 illustrations including 56 colored illustrations. Springfield, Illinois, & Baltimore: Charles C. Thomas, 1938.

This work, sumptuously illustrated in color and black and white, is a study of the results obtained by injecting suspensions of Higgins' engrossing ink into arteries and solutions of Berlin blue into veins. The only variation from standard injection methods was the use of high pressures: from 800 to 1,000 mm. of mercury in the injection of coronary arteries up to 1,500 mm. of mercury in the injection of leg vessels. After injection, the tissues were cleared by the method of Spalteholz. The illustrations are for the most part drawings, with photomicrographs, some by the Kodachrome method, and photographs. There are many picturesque drawings of the various capillary and sinusoidal systems found. The authors were influenced by a hope that they could demonstrate intimal vessels in normal arteries, which previous workers had failed to do. Their work furnishes added evidence, if any were needed, that the intima of normal arteries is not vascularized, since all the illustrations of injected human arteries showing intimal vessels are the seat of advanced atherosclerosis.

Much stress is laid on the finding of hemorrhages in some atherosclerotic lesions. It is difficult to follow the reasoning of the authors that these hemorrhages may have an etiologic relation to the disease atherosclerosis. The hemorrhages arise from vessels of capillary systems that are produced to supply nutrition to atherosclerotic lesions, as these enlarge beyond the possibilities of support by diffusion through the intima. In other words, the lesions in which capillary systems are found are already advanced lesions. How hemorrhages into advanced lesions can be etiologic factors in atherosclerosis is not explained.

The possibility that infection may be the etiologic factor in atherosclerosis is again presented, despite the contrary opinion of authorities, almost without exception, who have studied this disease. The authors refer to two early papers from the University of Oregon supporting this thesis but do not refer to a later paper from the same laboratory (Menne, F. R.; Beeman, J. A. P., and Labby, D. H.: Cholesterol-Induced Arteriosclerosis in Rabbits, with Variations Due to Altered Status of Thyroid, *Arch. Path.* 24:612 [Nov.] 1937) in which it is concluded: "In our considerations it seems evident that many agencies of disease, the variations in diet, the disturbance of internal secretions, infections, the traumatism of certain occupations and the influence of posture all aid in the development of arteriosclerosis only as they modify these two basic factors of hypercholesteremia and mechanical strain."

The bibliography on nutrition of the blood vessel wall by Dr. Elizabeth M. Ramsey, which is republished (*Yale J. Biol. & Med.* 9:13 [Oct.] 1936) as an appendix, is thorough. On the other hand the bibliography on arteriosclerosis lacks reference to many modern papers.

The book has value only as a study of the vascularization of advanced atherosclerotic lesions. Inferences are drawn that are not justified by the material presented and that tend to confuse the issue with respect to etiology.

The publisher is to be complimented on the makeup of the book, the reproductions and the clear type. The drawings are excellent.

**Les réactions d'équilibre chez l'homme: Étude physiologique et clinique des réactions d'équilibre sur la table basculante.** Par Jules Zador. Préface de M. André-Thomas. Paper. Price, 80 francs. Pp. 255, with 214 illustrations. Paris: Masson & Cie, 1938.

In this monograph Zador has attempted to extend to the clinic the experimental studies of Rademaker on equilibration, as Rademaker and Garcin had done previously. In his study he used a horizontal table on which the subject was placed in various positions, supine, prone, on the hands and knees or the elbows and knees, sitting and standing. The table was so constructed that it could be suddenly tilted, at first in only two directions about a single horizontal axis, but in a later model in four directions. The author accepts and bases his work on Rademaker's conclusions that the reactions which occur following sudden tipping of the table are labyrinthine in origin and following slow tipping are proprioceptive in origin. He is concerned only with the former and further quotes Rademaker to the effect that the reaction following sudden tipping is divisible into three phases: the labyrinthine, the passive, imposed by gravity on the body, and the proprioceptive.

He reports his observations on the normal adult in which the reaction can be simply stated as a tendency for the body to attempt to maintain the position present before the table tipped. In the infant he finds that by the age of 8 months the child attempts to maintain his position on the table but that the reaction until the age of 6 years is different and after that age is comparable to the normal adult reaction. He then records his results in a variety of pathologic conditions, disturbances of the vestibular nerves, cerebellar disease, cerebellovestibular syndrome, tabes dorsalis, hemiplegia without "static ataxia," extrapyramidal hyperkinesia, parkinsonism, catatonic stupor of dementia praecox and idiocy. In this section the book is most unsatisfactory. The clinical information is brief and often absent, and anatomic confirmation of the clinical diagnoses is wholly lacking. The reader is forced to accept the author's or his colleagues' interpretation of the cases. Such, of course, is very inconclusive and unsatisfactory in a monograph which poses as the presentation of a piece of human neurophysiologic investigation and presumes to offer a new technic for the examination and diagnosis of cases of nervous disease.

The author states that with bilateral involvement of the vestibular nerve the normal reactions are lost. They may be lost with a unilateral lesion, but compensation tends to occur and after a time the normal response may return. With chronic cerebellar disease the normal reactions are retained. Experience with acute cerebellar lesions is too limited to justify any statement and the method is not applicable to cases of tumor. With tabes dorsalis and catatonia the reactions are normal. With "extrapyramidal hyperkinesia" and in idiots the reactions revert to the infantile type. There is no index.

**The Essentials of Human Embryology.** By Gideon S. Dodds, Ph.D., Professor of Histology and Embryology, School of Medicine, West Virginia University, Morgantown, West Virginia. Second edition. Cloth. Price, \$4. Pp. 316, with 182 illustrations. New York: John Wiley & Sons, Inc.; London: Chapman & Hall, Limited, 1938.

This is a clear and simple presentation for the use of medical students of the facts and point of view which are essential for any understanding of human anatomy. It is prefaced by an excellent discussion of the physiology of reproduction in mammals as it is understood at the present moment. The theorizing and comparisons so dear to the heart of the embryologist are reduced to a minimum. This goes too far sometimes. The human yolk sac, for example, is dismissed as a "relic." At the eight weeks stage, to be sure, it seems to be nothing more than a useless vestige, but when one considers that during the third and fourth weeks the embryo takes form as it is spread out on the surface of the yolk sac precisely as in reptiles and birds, it is obvious that the yolk sac could not have dropped out of the life history of man without fundamentally modifying the whole scheme of development. Mention is made later of it as a hematopoietic organ; up to the fifth week it is the hematopoietic organ *par excellence*. Similarly, the pronephros and mesonephros have persisted through the ages because they are essential not only for the development of the wolffian duct but for

maintaining the patency of the duct and later the urogenital sinus (Boyden). The illustrations are done in the British manner—simple line drawings free from all ambiguity. Few create false impressions. The wofully incorrect figure of the "Bulle" embryo is here as in so many other textbooks. Figure 12 gives an erroneous idea of the character and mode of spread of the implantation syncytium. The chapter on the nervous system is written from the point of view of the neurologist, which is quite unusual in works on embryology. Books of this sort are good if the instructor points out that human embryology is not as fully worked out as the text seems to indicate. He does point out that the mechanism of development is still largely a mystery, but it would have been possible to say that recent experimental studies have revealed at least some of the factors concerned in normal development.

**Life, Heat, and Altitude: Physiological Effects of Hot Climates and Great Heights.** By David Bruce Dill, Fatigue Laboratory, Harvard University. Cloth. Price, \$2.50. Pp. 211, with 25 illustrations. Cambridge: Harvard University Press; London: Oxford University Press, 1938.

There seems no great justification for the publication of this volume. From a medical or scientific standpoint, Dill's material on the physiologic effects of high temperatures and high altitudes has already been well presented in readily available journals and its points of practical importance have been widely appreciated. Insufficient linkage exists between heat and the effects of altitude to justify his attempt at unified presentation. The chapter on desert animal life is interesting. The first sections on heat deal almost exclusively with effects on the water and salt balance and on the circulatory system, neglecting entirely the changes in internal combustion and in adrenal function that are brought about by adaptation to difficulty of heat loss. Desert animal life the author oversimplifies by division into those forms which obtain their water supply from plants and those which take it as free water. Surely there are all degrees of intervening gradation, just as exist in nondesert regions. And in his final sections on altitude effects no attention is devoted to barometric pressure as such, all observations centering around the results of oxygen deprivation. The presentation presumes to be physiologic in character, but only in the technical parts dealing with water and salt balance at high temperature and with the effects of low oxygen tensions is the material adequately handled. The medical reader will find in the book little of value that has not already been well stressed in scientific and medical journals, while for the layman the technical material and presentation make reading difficult and uninteresting.

**The Occupational Treatment of Mental Illness.** By John Ivison Russell, M.B., Ch.B., F.R.F.P.S., Medical Superintendent, North Riding Mental Hospital, Yorkshire, England. With foreword by William Rees-Thomas, M.D., B.S., F.R.C.P., Senior Medical Commissioner, Board of Control. Cloth. Price, \$2.50. Pp. 231, with 41 illustrations by Joseph Blagdon Morgan. Baltimore: William Wood & Company, 1938.

In the foreword of this interesting book by an English physician there is a quotation from Dr. Samuel Tuke of York Retreat, written in 1841, in which he gave credit to Sir William Ellis for introducing work on a large scale to asylum patients in England well over a century ago. But to Dr. Simon of Gutersloh is given the credit, early in this country, for using work as a "soothing potion in the hands of every nurse."

The purposes and aims of occupational therapy are discussed in the introduction. These deal freely with human nature, especially as it may react to success or failure. The value of work treatment does not depend on the quality of the thing made but more on the favorable reactions of the patient. The ability to work is usually a more wholesome commentary on recovery from fatigue than almost anything else that may happen.

Under psychologic types, motives for work are discussed—among others to serve, to delight, to rule. Some handle material things, as a curator; some work with symbols, as the clerk; others tend animals, such as fanciers; some serve human beings, as nurses. Interesting case histories of various clinical reaction groups are presented to demonstrate how work has blended into the lives of patients to alloy a better compromise between health and disability. In many respects the chapter on the prescription is the most interesting. Physicians gen-

erally do not give sufficient thought to the purpose of work to formulate a satisfactory program. An ingenious form is presented enabling a prescription to be written in code form covering aims to be achieved and dangers to be avoided.

The author discusses the degree of specialization among therapists found in Germany, the Netherlands and the United States. He leads one to believe that occupational therapy should be less specialized and more a part of the regular nursing regimen. It is refreshing to know that occupational therapy embraces a great variety of work, games, hobbies, dancing, entertainments and reactional activities indoors and out, including habit training. Spontaneity is emphasized. Formalism is decried. Work for the institution is no less valuable than anything else. Whether it should be centralized or scattered depends on local conditions, but in general there should be a well recognized headquarters for work. Some chapters are devoted to special buildings and facilities, the care and selection of supplies, and the choice of designs. Short chapters devoted to individual crafts give a simple statement of essential needs.

A chapter or two correlating work therapy with psychotherapy and hydrotherapy would have added to the value of the book; also a follow-up study to ascertain what place occupational therapy holds in the retrospective memory of socially adjusted patients.

The book is well written and illustrated and has much in it that commends itself to psychiatrist, nurse and occupational therapist, whether these are separate persons or one.

**Eine experimentelle Studie über Calciumoxalat als Steinbildner in den Harnwegen: Speziell mit Rücksicht auf die Bedeutung des Magnesiums.** Von Greta Hammarsten. Aus dem medizinisch-chemischen Institut der Universität Lund. Paper. Pp. 155, with 40 illustrations. Lund: C. W. K. Gleerup; Leipzig: Otto Harrassowitz, 1937.

This is a monograph in which the role of calcium oxalate in relation to stone formation in the urinary tract is exhaustively studied. Many tables are presented in demonstrating the physical properties of calcium oxalate in relation to solubility. The various effects of magnesium intake and urinary magnesium excretion on the formation of calcium oxalate stones are forcefully stressed. In animal experiments using rats, stone formation was frequent when the urinary magnesium excretion was lowered with coincidental increased calcium and oxalic acid excretion. However, if vitamin A and D deficiency was added to the foregoing conditions, stone formation was still greater and damage to the renal parenchyma more marked. An acid producing diet reduced definitely the incidence of stone formation. The frequency of stone formation in a large series of animals was greater in the male, coinciding with a higher urinary calcium output in the male sex. Males showed in general a higher urinary calcium excretion. It is interesting to note that on a vitamin poor diet with very low magnesium intake the incidence of stone in the female approaches that in the male. The view that protective colloids have no demonstrable part in the prevention of stone in either sex is maintained. Experimental stones were decalcified when the diet was changed to include adequate vitamins, calcium and magnesium, provided the renal parenchyma had not been too badly damaged. The more important clinical conditions under which calcium metabolism may be disturbed, often with increased urinary calcium excretion, are (1) calcium deficiency, (2) magnesium deficiency, (3) acidosis, (4) avitaminosis A, B, C and D, (5) hypervitaminosis A and D, (6) hyperparathyroid and hyperthyroid function, (7) intestinal diseases in which the absorption of the necessary minerals and vitamins is impaired, and (8) skeletal trauma of considerable extent. Stress is laid on the fact that even with a large intake of calcium and magnesium, unless they are in a readily absorbable form, deficiency of these substances will be evident. It is erroneous to assume that calcium containing foods are to be avoided in the presence of calcium stones. If sufficient calcium in an easily absorbable form, the best of which is milk, is maintained in the diet, along with an adequate magnesium and vitamin intake, a calcium balance is maintained, keeping the excretion of calcium in the urine very low. Conversely, a paradoxical increase in calcium excretion in the urine can be maintained by too

low a calcium intake with a concomitant deficiency in fat soluble vitamin ingestion. Foods rich in oxalic acids, which are tabulated, should be avoided. A bibliography which includes more than 300 references is included in this excellent work.

**A Textbook of Physiology.** By William D. Zoethout, Ph.D., Professor of Physiology in the Chicago College of Dental Surgery (Loyola University). Sixth edition. Cloth. Price, \$4. Pp. 714, with 291 illustrations. St. Louis: C. V. Mosby Company, 1938.

This edition of a popular intermediate textbook in physiology is in several respects an improvement on previous ones. The hormones and vitamins are more adequately treated than before. The section on higher central nervous system activity is particularly clearly written. The occasional phonetic analysis of words, as on page 170, is, however, of questionable propriety. A student sufficiently advanced to read the book should be acquainted with such words. A number of illustrations of out of date apparatus are still included, for example one of Dudgeon's sphygmograph. In general the illustrations are well selected and competently reproduced. There is a twenty page index which is well organized. A particularly distressing thing about the book is that the publisher's "blurb" on the jacket is a model for rhetorical errors and is in bad taste generally. Such statements as "In fact the entire make-up of the book was that good that it was used in schools in every state in the country with the exception of one" might easily deter one from looking seriously at the book itself.

**The Living Body: A Text in Human Physiology.** By Charles Herbert Best, M.A., M.D., D.Sc., Professor and Head of Department of Physiology, University of Toronto, Toronto, Canada, and Norman Burke Taylor, M.D., F.R.S., F.R.C.S., Professor of Physiology, University of Toronto, Toronto, Canada. Cloth. Price, \$3.60. Pp. 563, with 283 illustrations. New York: Henry Holt & Company, 1938.

This book was written for the college student and the inquiring layman and, as far as textual material and information go, is but another textbook since it does not present any particularly new approach or any original point of view over any of those in the several textbooks now available. The information is conventionally sound and simply presented. Illustrations cover much the same ground as found in any good textbook, although many are original; others were taken from well recognized and authoritative sources, all of which are acknowledged in the preface. These critical statements need not be interpreted as derogation, for the work is unquestionably valuable, but rather as decrying the current tendency to produce more and more textbooks for which there is no real demand and which do not offer any improvement over many of those already available. Taken alone, there is nothing to criticize in this book. Taken with other current textbooks, there is nothing in particular to praise.

**The Hypothalamus: Morphological, Functional, Clinical and Surgical Aspects.** By W. E. Le Gros Clark, D.Sc., F.R.C.S., F.R.S., John Beattie, M.D., D.Sc., George Riddoch, M.D., F.R.C.P., and Norman M. Dott, F.R.C.S. Ed. The Henderson Trust Lectures, Nos. XIII-XVI, published for the William Ramsay Henderson Trust. Cloth. Price, 12s. 6d. Pp. 213, with illustrations. Edinburgh & London: Oliver & Boyd, 1938.

This book, which is attractively bound, is printed on excellent paper and is well illustrated and contains four lectures which comprise the Henderson Trust Lectures delivered in Edinburgh in October 1936. The lectures have been enlarged to bring down to date the knowledge concerning the morphologic, functional, clinical and surgical aspects of the hypothalamus. Every one interested in organic neurology, endocrinology and neurosurgery will find this a comprehensive review of the subject. It is written by men who are well qualified; the authors admit our limited knowledge but present clearly and concisely what is known. The anatomic relations of the hypothalamus are described and a comparison between man and lower mammals is used to emphasize similarities and differences. The lecture on the functional aspect of the hypothalamus is of clinical interest, as it is divided into sections dealing with known physiologic evidence pointing to definite functions. The lecture on the clinical aspects of hypothalamic derangement outlines the so-called 'hypothalamic syndrome,' consisting of obesity, amenorrhea, diabetes insipidus, glycosuria and disorders of sleep. The

intracranial diseases which give rise to the hypothalamic syndrome are also described and discussed. Closely related to the clinical presentation is the lecture on the surgical aspect of the hypothalamus, in which cases are presented, with roentgenograms of the skull, ventriculograms, reproductions of photographs of the patients and drawings of the tumors found at operation. When the book has been read, one feels that the subject has been clearly, concisely and comprehensively presented in such a manner that every practitioner of medicine interested in the subject should consider it for his book shelf.

**The Construction of Vulcanite Applicators for Applying Radium to Lesions of the Buccal Cavity, Lips, Orbit and Antrum.** By Desmond Greer Walker, M.A., M.Dent.Sc., M.B., Assistant Dental Surgeon to the Royal Dental Hospital, London. Foreword by W. Warwick James, O.B.E., F.R.C.S., L.D.S. Published for the Middlesex Hospital Press. Cloth. Price, 5s. Pp. 61, with 23 plates. London: John Murray, 1938.

The treatment of malignant diseases of the mouth requires very accurate application of radiation, especially when it is applied in the form of radium therapy. Without mastery of the necessary complicated technic its imperfect use has in the past resulted in definite damage to the bone. This type of injury may now be avoided by the use of protective shields. This monograph is offered by the author as the outcome of experience gained through three years of radium work at the Middlesex Hospital in London. The employment of vulcanite applicators is carefully described, and for physicians working in radium therapy it should prove exceedingly helpful. These applicators afford a means of applying radium to sites which were previously impossible to treat, for instance the neighborhood of the anterior pillar of the fauces. The method offers a great improvement in accuracy over previous technics, and better protection for the surrounding tissues is possible by incorporating lead in the applicator.

## Bureau of Legal Medicine and Legislation

### MEDICOLEGAL ABSTRACTS

**Workmen's Compensation Acts: Enucleation of Eye Resulting from Exposure to Light Incident to Electric Welding.**—The claimant, in the course of his employment as a ship fitter, for several periods of from one-half hour to one hour each, Dec. 28, 1934, was exposed to the bright glare of light incident to electric welding machines. He did not wear goggles or eye protectors. He was not engaged in the operation of the machines but his work took him into their vicinity. On the day when this happened he had a "grippy" feeling but he worked all day. His eyes, he claimed, were normal except that he had to use glasses to read or draw on blueprint, but then he used only ordinary reading glasses. On previous occasions when he worked with or close to electric welding machines he had suffered some irritation of the eyes, but on this day he felt no discomfort until on his way home after work. Then his eyes "felt like some one would take a handful of sand and throw it in your eyes and cause your eyes to water all the time." When he reached home his wife sent for the family physician. She made a potato poultice to ease the irritation of the eyes. Not because of any condition of his eyes, but because he was not responding satisfactorily to the treatment for grip, a second physician, Dr. Jameson, was called in. He, however, noticed the home made remedy applied to the eyes and ordered it discontinued, suggesting the use of mild protein silver and boric acid. As the eyes got no better an eye specialist, Dr. Semeley, was called January 4. Dr. Semeley saw the claimant again January 7 and instructed him to go to the Wills Eye Hospital. There he was treated by Dr. O'Brien, and after several weeks of observation and treatment Dr. O'Brien enucleated the claimant's left eye.

Claiming that the loss of his eye was due to exposure in the course of his employment to the flashes of electric light caused by the electric arc welding machines, the claimant instituted proceedings under the workmen's compensation act of

New Jersey. A referee for the workmen's compensation bureau denied him compensation. The claimant thereupon appealed to the court of common pleas of Camden County, which reversed the finding of the referee and awarded compensation. The claimant's employer then appealed to the supreme court of New Jersey.

Dr. O'Brien, who had treated the claimant in Wills Eye Hospital and who had enucleated his eye, testified that the claimant had suffered from panophthalmitis, which he described as an inflammation of all the structure of the eye from "within out." In his judgment the flashes of light from the electric welding had irritated the eyes of the claimant and caused him to rub them. By rubbing them he started up virulent organisms or sources of infection, present in almost every eye, and they "broke through" the front of the eye and infected the entire organ. In Dr. O'Brien's opinion the infection did not come from within the eye or from any source back of the eye; after removing the eyeball he had examined the eye socket and found no pathologic change in its bony framework. The infection did not come from the sinuses. Dr. Shemeley, who saw the claimant only twice, January 4 and January 7, testified on behalf of the employer. Although the claimant's exposure to the flashes from the electric welding process occurred on December 28 and this witness did not see him until January 4 and although the witness admitted that it was possible for a "flash burn" to clear up in twenty-four hours, he testified that in his opinion the condition of the claimant was not due to a flash burn. In the opinion of this witness the claimant's exposure to the flashes of light from a welding machine would not have any effect on his eye.

Another medical witness on behalf of the employer, who examined the claimant April 12, some months after the eye had been removed, and who based his opinion on symptoms and conditions stated in the notes made by Dr. Shemeley on the two occasions on which he saw the claimant, was of the opinion that the infection came from within and was not the result of the exposure to the flashes of light incident to electric welding.

In summing up, the supreme court emphasized strongly the differences in the opportunities that the several expert witnesses whose testimony is referred to had had for becoming personally acquainted with the condition of the patient. Dr. Shemeley had seen the patient only twice, "on both of which instances the organ was in a very distressed condition." Dr. Dublin's testimony was predicated on an examination made a considerable time after the claimant's eye had been removed and rested in the main on charts prepared by Dr. Shemeley. Dr. O'Brien saw the claimant daily for weeks, then removed the eyeball, and thereafter kept the claimant under observation. It is not necessary, said the court, for the claimant to carry the burden of proof to the point of demonstration. It is sufficient to show that the hypothesis on which he based his claim is probable, and this, the court thought, the claimant had done. For that reason the judgment of the court of common pleas of Camden County in favor of the claimant was affirmed.—*Jackson v. New York Shipbuilding Corporation* (N. J.), 197 A. 284.

**Dental Practice Acts: Suspension of License for Conviction of Crime; Subsequent Good Conduct as Mitigating Circumstance.**—Brown, a licensed dentist, was convicted of manslaughter and sentenced to pay a fine and serve a jail sentence. The jury recommended clemency and he was thereafter paroled. About a year and a half later, the board of governors of the registered dentists of Oklahoma suspended Brown's license under a provision of the dental practice act authorizing the board, on presentation of a certified copy of a court record showing that a licentiate has been convicted of a crime involving moral turpitude, to revoke his license or to suspend him from practice or to reprove him. Brown appealed to the Supreme Court of Oklahoma.

The evidence showed that Dr. Brown had practiced dentistry since 1911, that he had always borne a good reputation, that he was a man of good morals and high character, that the only blemish on his record was the act which formed the basis of

his conviction, and that subsequent to the conviction he bore a good reputation and maintained a high standing of character. One who has practiced his profession for twenty-three years, said the Supreme Court, maintaining at all times an excellent reputation and being in fact a man of high character, but who then is guilty of such an act of moral turpitude as was here charged against Brown, may thereafter so conduct himself by right conduct in his profession and as a citizen as to reestablish himself as a man of high character. This, in the opinion of the court, Dr. Brown had done. The board seemed to have concluded that the conviction required it to take disciplinary action without regard to the fact that subsequent to the conviction the dentist had conducted himself above reproach. That view, the court said, while doubtless entertained in good faith, was erroneous and in law constituted an abuse of discretion on the part of the board. The Supreme Court accordingly reversed the decision of the board suspending Brown's license to practice dentistry.—*Board of Governors of Registered Dentists of Oklahoma v. Brown* (Okla.), 76 P. (2d) 1074.

## Society Proceedings

### COMING MEETINGS

American Student Health Association, New York, Dec. 29-30. Dr. Ruth E. Boynton, Students Health Service, University of Minnesota, Minneapolis, Secretary.  
Pacific Coast Society of Obstetrics and Gynecology, Los Angeles, Nov. 30-Dec. 3. Dr. T. Floyd Bell, 400 29th St., Oakland, Calif., Secretary.  
Radiological Society of North America, Pittsburgh, Nov. 28-Dec. 2. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y., Secretary.  
Society for the Study of Asthma and Allied Conditions, New York, Dec. 3. Dr. W. C. Spain, 116 East 53d St., New York, Secretary.  
Southern Surgical Association, White Sulphur Springs, W. Va., Dec. 6-8. Dr. Alton Ochsner, 1430 Tulane Ave., New Orleans, Secretary.  
Western Ophthalmic Association, Omaha, Dec. 2-3. Dr. Albert H. Montgomery, 122 South Michigan Blvd., Chicago, Secretary.

### THE AMERICAN RHEUMATISM ASSOCIATION

*Fifth Annual Meeting and Seventh Conference on Rheumatic Diseases, held in San Francisco, June 13, 1938*

LORING T. SWAIM, M.D., Boston, Secretary

#### Radiculitis Associated with Spinal Arthritis

DR. WILLIAM J. KERR, San Francisco: The radicular syndrome has been described as a symptom complex associated with hypertrophic spondylitis or osteo-arthritis of the spine. The symptoms are related to local inflammatory or degenerative processes in the spinal column adjacent to or involving the nerve roots, causing sensory and motor disturbances of radicular distribution. In some cases the autonomic nerves are affected. The symptoms are dependent on movements of the spine, relaxation of the supporting spinal structures or circumstances which cause an increase in the intraspinal pressure. Among these are the acts of coughing, sneezing or straining at stool (Dejerine's sign).

The symptoms are referable to the nerves emerging from the spinal axis. Disturbances in sensation, spasm of muscles with limitation of motion of the spine and atrophy of skeletal muscles are of common observation. These changes are evidently related to injury of the skeletal nerves. Other disturbances in the viscera and to the vessels of the trunk and extremities are related to injury of the autonomic nerves supplying these structures. Vascular symptoms in the extremities may precede swelling in the joints in some cases, suggesting that the involvement of the joint is likewise due to irritation of sympathetic nerves at the spinal axis. Any segment of the body may be affected. Those regions from which the nerves supplying the extremities emerge from the spine appear to be most frequently involved. Perhaps this is only because we are more able to recognize the patterns of symptoms related to lesions in these regions.

Altered sensations are commonly observed. Hyperesthesia or hypo-esthesia to light touch (cotton wool), to painful stimuli or heat and cold may be demonstrated by careful study of the segments involved. Pain or tenderness on pinching of the skin

may help to localize the radicular area affected. Hypertonus of the muscles in the early stages and hypotonus or atrophy in the late stages may be helpful. Any condition which increases the intraspinal pressure, e. g. pressure on the jugular veins (the Queckenstedt test) or coughing, sneezing or straining at stool, may reproduce the symptoms. This test thus is not a differential test from tumor of the spinal cord or nerve roots. The pain may be relieved by vasodilators such as amyl nitrite or glyceryl trinitrate and thus with pain simulating angina pectoris the differentiation cannot always be made by these drugs. If the symptoms are abdominal one may put the abdominal muscles on tension, and tenderness on palpation will disappear, whereas in peritonitis the tenderness will persist.

The segmental areas involved will generally direct attention to the segments of the vertebral column which are involved. Local tenderness of the spine, pain on motion and stiffness of the spinal column may be found if the process is active or recent, or rigidity may exist without other signs if the process is quiescent. Films of the spine may show few changes early when symptoms are acute but generally there is some evidence of changes in shape or density of the bodies of the vertebrae or intervertebral disks, some fuzziness or narrowing of the foramina, or spurring of the margins of the vertebrae or the articular facets with the ribs. Changes in the spinal curves and scoliosis may be shown best by films. In some cases marked osteo-arthritis changes are shown by x-ray examination when there are no symptoms. Almost invariably there are detectable signs and the patient has forgotten the acute manifestations.

The treatment is effective in many cases. In patients whose occupations place undue strain on certain parts of the spine, some relief may be obtained by changing to another occupation which puts less strain on the spine. The most frequent contributing factor is distortion of the spinal column by excessive weight on the trunk. The pendulous abdomen accentuates every curve. The lower lumbar and lumbosacral and sacro-iliac joints suffer most but compensatory changes in the upper thoracic and cervical spine usually give symptoms in the upper extremity or in the upper cervical region, with frequent radicular symptoms in the occipital region. Abdominal support and dietary management frequently relieve the symptoms in this group.

Temporary symptomatic relief may be obtained from drugs (salicylates) or from local heat, which may be moist heat, radiant heat, electric pad or the use of a hot electric iron or flat iron moved back and forth along the spine over several thicknesses of a bath towel. Gentle massage and manipulation may be helpful. In some cases of cervical arthritis, stretching of the neck may be resorted to with great relief. Other more radical measures are generally unnecessary. Violent manipulations have been known to cause fractures of the vertebrae or their processes and therefore those who practice spinal adjustments should be avoided. The orthopedists are learning to treat these patients more rationally and often with great benefit, but other specialists in the surgical field have much to learn about the diagnostic features of the syndrome. The abdominal scars, often multiple, seen on many of these patients bear testimony to hasty judgment in the interpretation of symptoms.

#### Nonrheumatic "Growing Pains" and Subacute Rheumatic Fever

DR. M. J. SHAPIRO, Minneapolis: Painful extremities in children have been given a variety of names, such as growing pains, muscular rheumatism and muscle and joint pains. In a number of recent articles from 8 to 50 per cent of children considered as rheumatic have been so diagnosed on the basis of pain in the extremities alone. Actually, an analysis of the histories of 100 of the patients with well developed rheumatic heart disease at the Lymanhurst Health Center reveals that 84 per cent of them gave a definite history of a major attack of rheumatic infection: either rheumatic fever or chorea, or both. A critical study of the remaining 16 per cent demonstrates that in practically every instance, in spite of the fact that no history of a major attack of rheumatic infection was obtained, there was definite evidence that they were suffering from a long continued rheumatic infection. They presented the well known signs and symptoms of chronic rheumatic infection, such as low grade fever, loss of weight, definite joint pains, nosebleeds, skin

rash, increased sedimentation rate and pallor, although their symptoms were not severe enough to put them to bed.

A follow-up study on 200 children who complain only of leg pains has been carried out at the Lymanhurst Heart Clinic for the past three years. None of them have presented any evidence of chronic rheumatic infection. They complain of pain primarily in the lower extremities. The pain comes on commonly at the end of the day and often awakens the patient during the night. They rarely complain of pain during the day and practically never have symptoms in the upper extremities. They are usually in good health otherwise, and none of them have developed rheumatic heart disease. Laboratory studies of these patients give normal results. This syndrome is so common in healthy school children during early childhood and adolescence that it is suggested that their complaint is due to normal growth. It is clear that they are not suffering from rheumatic fever and should not be so considered.

Many children with growing pains alone have been subjected to tonsillectomy, sinus drainage, periods of rest in bed, vaccine treatment, and so on on the erroneous conception that they were suffering from rheumatic fever. It would appear that the old idea that normal growing children do suffer from growing pains is probably correct. Much of the confusion could be avoided if the term "growing pains" was not used in connection with rheumatic fever.

#### DISCUSSION

DR. T. DUCKETT JONES, Boston: This report should do much to clear up the vagueness which exists concerning the joint manifestations of rheumatic fever. Especially harmful has been the attempt to label a child as prerheumatic with little or no justification. The absence of a specific diagnostic test is the cause of the difficulty. The development of heart disease of the rheumatic type is the most definite existing proof that a child has had rheumatic fever. In my experience, definite arthralgia has occurred at some period of active rheumatic fever in fully 70 per cent of a large series. The type of pain has been well described by Dr. Shapiro. Joint symptomatology may be real, but it is rarely of a chronic nature, and other features are much more significant. I should heartily agree with Dr. Shapiro that so-called growing pains in a child, without a frank history of previous rheumatic fever, do not frequently occur with other manifestations of rheumatic fever or a tendency to develop subsequent rheumatic heart disease. This has proved to be true even in families in which there are one or more definite rheumatic fever subjects. It is common today to see definite rheumatic fever with the development of rheumatic heart disease, without joint symptomatology, at the time of acute illness. Abundant clinical and laboratory evidence supports this view. In the carefully followed rheumatic child, mild to severe acute illness is almost invariable, and vague syndromes rarely exist. The insidious or asymptomatic development of rheumatic heart disease in children is uncommon, but in the young adult it is observed. This demonstrates that silent rheumatic fever does exist, but in following such a group I have been impressed with the frequency with which abnormal laboratory data are found either by electrocardiogram or by such nonspecific measures as the white blood count or sedimentation rate. Dr. Shapiro has noted that these tests are normal in children with growing pains, and this would seem significant to me. I should like to ask Dr. Shapiro whether he has followed any appreciable number of children with vague muscle aches and pains for a significant period of time? Dr. Shapiro's differentiation is not only important to the problem of the individual child but should help us in the broader aspects of the problems of rheumatic fever. Especially, it should help prevent the partial invalidism and even institutional care of a large group of children so often mistakenly thought to have rheumatic fever.

DR. J. ALBERT KEY, St. Louis: I am glad that the growing pains are coming back again. I have told the parent "this child has growing pains" and had them reply "I am sorry, but my doctor tells me that growing pains are old fashioned and they don't have them any more." As a matter of fact, people do have growing pains. Most growing pains, I think, are not to be classed as epiphysitis but as epiphysal strains. It is also conceivable, as Dr. Hitchcock just suggested to me, that growing pains are due to a strain of muscles: bones may grow faster



than muscles and fascia and cause strains at the muscular attachments. A third explanation is that they may be due to actual stretching of the nerves due to rapid growth of bones.

DR. M. HENRY DAWSON, New York: Could it be found whether an actual quantitative study has been done on growth during that period in which growing pains occur? Do the pains occur most frequently in individuals who grow most rapidly?

DR. FRANKLIN R. NUZUM, Santa Barbara, Calif.: As an index of how prevalent the belief is that growing pains in children do mean rheumatic fever, I reviewed six current medical textbooks and found that three of them stress the importance in the history of the occurrence of so-called growing pains in arriving at a diagnosis of rheumatic fever. Dr. Shapiro, on the other hand, has shown that among his own patients this type of pain occurs in healthy growing children. He has further substantiated his argument by following for a period of years a group of children that were referred to him with a diagnosis of rheumatic fever and whose chief complaints were "growing pains." He found that other symptoms of rheumatic infection did not develop: laboratory tests were negative, their symptoms continued to or through adolescence and disappeared, and further repeated examinations after a period of years demonstrated that rheumatic heart disease had not developed in any of this group. The latter is a most convincing point, since approximately 75 per cent of children with rheumatic infection do develop clinical evidence of heart disease. Just as it is incorrect to attach the stigma of rheumatic fever to a child who complains of muscle pains occurring especially at night, so is it incorrect to give the name rheumatic fever to the secondary arthritides that may complicate scarlet fever, pyemia, cerebrospinal fever, dysentery and other acute infectious diseases. When a single articulation is affected in a child, the condition rarely is due to rheumatic fever. The same is true of the disorder of more than one joint that remains stationary for many days, especially in the first attack. The intervertebral articulations are seldom involved in rheumatic fever but often are involved in tuberculosis and gonorrheal infections. It is generally believed that every child who has rheumatic fever suffers some damage to the heart. In about 75 per cent the degree of inflammation is sufficient to result in evident damage to the valve leaflets, the heart muscle or both. In those instances in which physical examination does not elicit evidence of heart damage, an electrocardiogram may be used as an aid in making the differentiation between rheumatic fever and recurring muscular pains of other etiology. In the former, abnormal curves are obtained in about 90 per cent; in the latter, normal curves are usually found. The abnormal electrocardiograms present a variety of changes; among them, a delay of conduction time between auricle and ventricle, abnormalities of the P or auricular wave, and/or of the RS-T or ventricular segment. The importance of an accurate history as an aid in arriving at a diagnosis of rheumatic fever bears emphasis. Dr. Shapiro has implied that this part of the study should not be detailed to a nurse assistant or an intern but should be carried out by the physician himself.

DR. M. J. SHAPIRO, Minneapolis: I have consulted a number of investigators interested in the study of growth and have tried to get an opinion on this subject. They all agree that normal growth might possibly produce such symptoms but they would not commit themselves. I have made no claim that this clinical entity is due to growth. I suspect that it is, because it is so common. Those of us who have been working on the subject of rheumatic fever are, I believe, responsible for most of the errors that are made. We have carried on propaganda for many years to impress the public with the idea that there was no such thing as "growing pains," that growth was painless, and that "growing pains" in most instances were manifestations of rheumatic fever. As Dr. Key has stated, many children with "growing pains" are referred to private physicians and clinics with a previous diagnosis of rheumatic fever. In answer to Dr. Jones's question as to how long these patients had been followed, I may state that this study was set up three years ago. All patients with "growing pains" who in my opinion were not suffering from rheumatic fever have been included in this group. The clinical picture is so similar that statistical study seems hardly necessary although it is admitted that these patients have not been followed long enough. Up to the present time, none

of them have developed rheumatic heart disease. As Dr. Dawson has pointed out, it will be of considerable interest to determine whether or not these children have most of their symptoms during the period of most active growth. Such a study is now being carried out.

#### Metabolic Factors in the Induction of Carditis

DR. MARK P. SCHULTZ, Washington, D. C.: Nonpurulent carditis was induced in rabbits and guinea pigs subject to chronic focal, hemolytic streptococcus infection while being treated with moderate doses of thyroid; suitable controls were negative. When dinitrophenol was substituted for thyroid under similar conditions, no cardiac lesions resulted. In guinea pigs affected with chronic focal infection while receiving maximum tolerated doses of insulin, valvular and myocardial lesions developed similar to those observed in infected, scorbutic animals: the association here of scurvy as a complicating factor was improbable. An attempt was made to determine which of several attributes of the scorbutic state are factors in the development of nonpurulent carditis during the course of associated focal infection; viz., acidosis, adrenal damage or increased metabolic rate. The hearts of guinea pigs with chronic focal infection forcibly fed large doses of acidic salts were negative. No cardiac lesions were observed in adrenalectomized rats with chronic focal infections. The nonpurulent carditis observed in infected guinea pigs with chronic scurvy was of greatly increased incidence and severity in such animals treated concurrently with ultraviolet irradiation to enhance further their metabolic rate above that degree of elevation associated with uncomplicated scurvy. The increased metabolic rate in scurvy is probably a factor in the induction of nonpurulent carditis during the course of infection.

These experiments demonstrated that the induction of various metabolic anomalies in experimental animals during the course of chronic focal infection conduces to the development of nonpurulent carditis. In this connection the possible significance was suggested of the relatively frequent development of rheumatic fever and exophthalmic goiter in the same individuals and the cessation of rheumatic fever activity in those patients developing diabetes.

#### DISCUSSION

DR. K. K. SHERWOOD, Seattle: These experiments show that part of the result is due to the metabolic state of the animal at the time of the experiment. I should like to ask the author whether he subscribes to the view that this increased metabolic rate automatically increases the vitamin C requirement. In relating these experiments to the clinical problem, the question arises as to the absorption of the available dietary vitamin C. We know that human beings with atrophic arthritis and rheumatic fever frequently require an extremely high vitamin C intake for a long time before it becomes reflected in the blood level. The third question concerns edema in low vitamin C states. It seems to me that part of the therapeutic effectiveness of vitamin C lies in a partial control of edema in certain rheumatic states.

DR. JAMES F. RINEHART, San Francisco: The interpretation of Dr. Schultz's experiments is not easy. The production of a carditis in rabbits and guinea pigs treated with thyroxine or thyroid substance and subjected to streptococcal infection is probably explainable on the basis of an induced vitamin C deficiency incident to the action of the thyroid substance. Schuelter found that thyroid depleted the organ content of vitamin C while dinitrophenol did not have this effect. If the augmentation of the nonpurulent carditis of scurvy and infection by irradiation induces a hyperthyroid state with the increased activity of the heart, one would expect an augmentation of the carditis. The possibility of irradiation introducing another toxic influence must be borne in mind. The experiments with insulin are more difficult to interpret. However, it would appear pertinent to investigate the effect of prolonged large doses of insulin on the vitamin C metabolism. I believe the induced cardiac pathologic conditions in this series of experiments was less striking than in the thyroid experiment and I am not agreed that they resemble those of rheumatic fever as closely as those of scurvy and infection. In my experience significant cardiac lesions resulted only from the combined influence of infection (chiefly of the hemolytic streptococcus type) and vitamin C deficiency and rarely if at all in uncomplicated vitamin C



deficiency. The experimental production of a carditis and arthritis and the occasional development of subcutaneous nodules affords an unusually broad experimental basis for the thesis that vitamin C deficiency enters in the etiologic mechanism of rheumatic fever. Metabolic studies indicate that depletion of vitamin C is the rule in rheumatic fever. The concept that vitamin C deficiency contributes to the etiology of rheumatic fever has as yet been inadequately investigated in the clinic. Well controlled and prolonged therapeutic and prophylactic experiments remain to be done and to me appear clearly indicated.

DR. J. ALBERT KEY, St. Louis: Since it is conceded that with infection there is an increased demand for vitamin C, it is possible that here the infection may be the primary factor. It also appears to me that possibly the thyroid which was given acted as a direct toxin on the heart and that the reason these animals developed carditis was that their heart was damaged and the organisms attacked the point of lowered resistance. It is also important to know what other lesions these animals had in addition to their carditis. It may be that these experiments reduced their general resistance much as Pasteur did when he had his chickens stand in cold water. Finally it should be pointed out, as Kinsella noted last year before the Association of Physicians, that the primary lesion in rheumatic fever is not a purulent lesion. There is considerable difference between the primary lesions in rheumatic fever and the primary lesion induced by any known streptococcus. In a streptococcal infection the primary cell reaction is a polymorphonuclear leukocyte infiltration in the damaged area and, as I understand it, in rheumatic fever this does not occur. I don't think that we have the right to correlate a late fibroma induced by any means whatever with rheumatic fever because it resembles a late rheumatic lesion.

DR. T. DUCKETT JONES, Boston: Dr. Schultz's work has been presented in a straightforward manner, and no involved claims concerning etiology were made. A most salutary phase of the work is that it carries to the laboratory some of the features observed in patients with the disease in question. It should stimulate further attempts to reproduce rheumatic fever experimentally by means of variations and features observed at the bedside. There has been a tremendous amount of experimental work with streptococci in the past forty years, without any proof that any form of streptococcus is the cause of rheumatic fever. This should not only make us critical of any new theories but spur us on to renewed effort along lines at variance with ordinary accepted ideas. It is pertinent to mention the work of Dr. Rinehart and his co-workers on the possible role of vitamin C in rheumatic fever. In our experimental studies with guinea pigs the same lesions were found in animals with acute scurvy as in those with chronic scurvy and superimposed streptococcal infection. It has seemed to us that the streptococcal infection produced a complete scorbutus and that this was responsible for the lesions in the guinea pig heart. Dr. Schultz has told me that he has been unable to confirm this observation and suggests as a reason the frequent finding of an unsuspected streptococcal infection in guinea pigs kept in the laboratory. This is a possibility, but more important would seem to be the distinct variations in diet used. It may be well to add a further word of caution concerning vitamin C, since it has been mentioned freely and may well be important in rheumatic fever. My remarks concern the obvious pitfalls in considering such features as the geographic distribution and seasonal incidence of rheumatic fever as furthering any particular etiologic hypothesis. The geographic incidence of rheumatic fever is unknown. We speak glibly of its absence in the South, and yet every intelligent survey in areas where the disease is thought to be nonexistent indicates the fact that the disease is present, though it may be uncommon. Just recently in southern Florida I have seen a number of natives with definite rheumatic fever. In this area fruit is cheap and sunshine abundant. Also hemolytic streptococcus infections in this area are uncommon. We have streptococcus immune body studies on a group in this community, and although respiratory infection is common, specific hemolytic streptococcus immune bodies rarely develop. It is not entirely reasonable, therefore, to consider the availability of inexpensive

vitamin C and the geographic distribution of rheumatic fever as necessarily being important from an etiologic point of view.

DR. DAVID FERGUSON, Bremerton, Wash.: Dr. Key brought up an important point in asking whether the pathologic condition found in the hearts of the animals that had thyroxine was not due to thyroxine rather than to infection. McEachern and his associates have definitely shown that focal necrosis as the pathologic lesion in thyroid heart disease does not occur. In fact, no anatomic changes occur in the heart as the result of hyperthyroidism. Dr. Schultz seems to show that there is some curious synergistic effect resulting from the combination of infection and thyroxine.

DR. MARK P. SCHULTZ, Washington, D. C.: I wish to emphasize the comment of Dr. Jones that the experimental lesions which have been described are not presented as those of rheumatic fever, although in my opinion they do somewhat resemble them. Concerning such experimentally induced lesions the conception is, of course, offered that the human disease is actually reproduced and that the failure to duplicate it actually is due to species differences in reactivity. It is doubtful that on the basis of the evidence at present available such a conclusion may be reached with respect to the observations which have just been presented. Dr. Sherwood has pointed out that coincident with an increased metabolic rate the vitamin C requirements of the organism are increased and that consequently the pathologic changes which were induced may have been occasioned by concomitant scurvy. In rabbits treated with thyroxine the validity of such a conclusion seems improbable, as this species belongs to the group not susceptible to such nutritional deficiency. The guinea pigs treated with insulin, it should be emphasized, received sufficient ascorbic acid subcutaneously to protect them in event of a complete absence of this vitamin from other sources against all the manifestations of scurvy except the microscopic tooth changes. In addition, because their appetites were inordinately increased and cabbage was liberally supplied in measured quantities, they are known to have consumed from eight to ten times the amount of vitamin C which has been found adequate to protect such animals against scurvy when no other source of the vitamin is present. The same is true of the rabbits and guinea pigs treated with thyroxine or desiccated thyroid gland. Dr. Heninger and others have recalled the fact that cardiac lesions resembling some of those which have been described here have been reported induced in experimental animals merely by treatment with thyroid and suggest that the results which have just been outlined were possibly due to an uncomplicated toxic effect of thyroid. I feel that this is unlikely for two reasons: First, a detailed study of the literature bearing on this point brings to light the fact that in most papers reporting the induction of damage to the heart through action of an excess of thyroid alone it is also reported, without particular significance being attributed to the circumstance, that accidental infection was present in the animals under observation. In studies such as those of Rake and McEachern, in which the presence of infection is rightly excluded during the period of thyroid treatment, no cardiac damage is observed. Second, the hearts of our control animals which received thyroid but were not infected were essentially normal. Dr. Jones and his colleagues and others have recently reported the development of cardiac lesions in guinea pigs of the type originally described by Dr. Rinehart and his associates, and of that under discussion here, in animals subject to scurvy not complicated by infection. My experience has been to the contrary, for the hearts of guinea pigs dying from the effects of scurvy have been essentially normal in those instances in which the presence of infection could be excluded with certainty. The wide prevalence of spontaneous hemolytic streptococcus lymphadenitis in guinea pig stock is probably responsible for the difficulty on this point. It has been my experience that positive cultures may be obtained from subcutaneous areas in the cervical, inguinal and axillary regions in many instances in which cultures of the blood and various internal organs are negative. Unless cultures are made from the parts mentioned it is improbable that the presence of infection can be excluded without question.

(To be continued)

## Current Medical Literature

### AMERICAN

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Titles marked with an asterisk (\*) are abstracted below.

#### Alabama State Medical Assn. Journal, Montgomery

8: 133-164 (Oct.) 1938

- Optimistic View of the Problems of Heart Disease. T. M. McMillan, Philadelphia.—p. 133.
- Present Status of Treatment of Pneumonias. O. W. Bethea, New Orleans.—p. 140.
- Infant Mortality. W. G. Casey, Talladega.—p. 144.
- Irritable Colon. I. C. Berrey, Birmingham.—p. 146.
- Treatment of Lobar Pneumonia. L. C. Davis, Gordo.—p. 150.

#### American J. Digestive Diseases, Huntington, Ind.

5: 461-548 (Oct.) 1938

- Carbonate Excretion in Urine as Indication of Alkalosis. L. C. Gatewood, Chicago.—p. 461.
- Variations in Enzymatic Activity of Duodenal Contents: Preliminary Report. V. C. Myers, A. H. Free and A. J. Beams, Cleveland.—p. 464.
- Triple Mechanism of Chemical Phase of Gastric Secretion. B. P. Babkin, Montreal.—p. 467.
- Present Status of Treatment in Chronic Gastritis: Gastroscopic Observations. W. A. Swalm and L. M. Morrison, Philadelphia.—p. 472.
- Psychiatric Contributions to Study of Gastrointestinal System. E. D. Bond, Philadelphia.—p. 482.
- \*Studies on Use of Aluminum Hydroxide Gel in Treatment of Peptic Ulcer. E. S. Emery Jr. and R. B. Rutherford, Boston.—p. 486.
- \*Level of Ascorbic Acid in Blood and Urine of Patients with Peptic Ulcer. D. T. Chamberlin and H. J. Perkin, Boston.—p. 493.
- Vagotomy Plus Partial Gastrectomy for Duodenal Ulcer. A. Winkelstein and A. A. Berg, New York.—p. 497.
- Development and Healing of Gastric Ulcer: Clinical, Gastroscopic and Roentgenologic Study. W. L. Palmer, R. Schindler and F. E. Templeton, Chicago.—p. 501.

**Aluminum Hydroxide Gel in Peptic Ulcer.**—Emery and Rutherford used colloidal aluminum hydroxide in the treatment of eight cases of the severe type and four of the moderately severe type of peptic ulcer. Five of the patients were treated by the drip method and seven by the oral method. Those patients who started on the drip method were shifted to the oral method after one week. A solution of one part of the aluminum hydroxide (creamalin) to three parts of water was used at all times. The amount which was used varied slightly, but on the average 15 drops per minute was allowed to drip through the tube. It was given orally in amounts of 60 cc. of the mixture per dose. A dose was given every hour from 8 a. m. to 9 p. m. In addition to the aluminum hydroxide, the patients were fed according to the schedule outlined by Sippy. All patients were relieved of pain due to the ulcer within twenty-four hours and had no recurrence of pain while remaining on the treatment. Colloidal aluminum hydroxide in addition to neutralizing the secreted acid decreases the titratable acidity of the gastric juice. Oral administration of the drug produces a somewhat slower decrease in the titratable acidity, which ultimately reaches the same general level. All patients who fail to respond satisfactorily to the Sippy regimen should be treated with aluminum hydroxide before surgical intervention is carried out. Colloidal aluminum hydroxide is also useful for treating ulcer patients who show a tendency to form renal calculi. The drug is absorbed but slightly and does not interfere with the acid base balance. It proved to be useful in treating four patients who had nephrolithiasis.

**Ascorbic Acid and Peptic Ulcer.**—Chamberlin and Perkin estimated the ascorbic acid in the blood of twenty-seven hospitalized patients with peptic ulcer. Lower levels of ascorbic acid were found in the blood and urine of these patients than in normal individuals or patients with functional digestive disorders. That patients with peptic ulcer require a greater

amount of ascorbic acid is demonstrated by the fact that daily medication with ascorbic acid results in an earlier and greater excretion of ascorbic acid in the urine of normal individuals and patients on other dietary management than in patients with peptic ulcer. The amount of additional ascorbic acid required to raise the excretion of ascorbic acid to normal in patients with peptic ulcer appears to be 50 mg. four times a day. It is suggested that the metabolism of ascorbic acid is influenced by activity and that lower blood and urine values are found in patients resting in bed than in active persons.

#### American Journal of Diseases of Children, Chicago

56: 723-956 (Oct.) 1938

- Reactions Following the Use of Diphtheria Toxoid: Analysis of Reactions and of Guides to Their Occurrence. C. R. Hayman, New York.—p. 723.
- Effect of Vitamin B<sub>12</sub> on Iron Retention of Normal Infant. F. W. Schlutz, Helen Oldham and Minerva Morse, Chicago.—p. 735.
- \*Cervical Rib in Early Life. D. B. Davis, New York, and J. C. King, Memphis, Tenn.—p. 744.
- Permeability of Blood Sulfocyanate Barrier to Sodium Bromide in Experimental Poliomyelitis. E. H. Lennette and D. H. Campbell, Chicago.—p. 756.
- Lead Poisoning: Report of Case, with Some Physicochemical Considerations. I. Kowaloff, Brooklyn.—p. 764.
- Making a Corrective Shoe. L. Bivings, Atlanta, Ga.—p. 775.
- \*Acute Bulbar Poliomyelitis Following Recent Tonsillectomy and Adenoidectomy. M. Stillerman, Great Neck, N. Y., and A. E. Fischer, New York.—p. 778.
- Copper and Iron in Human Blood: Comparison of Maternal and Fetal Blood After Normal Delivery and After Cesarean Section. A. Sachs, V. E. Levine, W. O. Griffith and C. H. Hansen, Omaha.—p. 787.
- Human Passive Transfer Antibody: IV. Studies on Children Hypersensitive to Foods. V. W. Lippard and W. M. Schmidt, New York.—p. 797.
- Effect of a Milk Supplement on the Physical Status of Institutional Children: III. Progress of Dental Caries. Lydia J. Roberts, Stella Englebrecht, Ruth Blair, W. Williams and Marguerite Scott, Chicago.—p. 805.
- Bronchiectasis in Children, with Special Reference to Prevention and Early Diagnosis. Antoinette Raia, New York.—p. 852.

**Cervical Rib in Early Life.**—Davis and King state that in the latter half of 1936 three children with cervical rib were seen at the John Gaston Hospital and at the outpatient clinic. This succession of cases suggested that similar cases might previously have been overlooked. Therefore 1,000 consecutive roentgenograms of the chests of children less than 13 years of age were studied. The incidence of cervical rib in the 1,000 consecutive roentgenograms was 1.2 per cent. Reproductions of the roentgenograms in the twelve cases are depicted. Ten of the cases were bilateral and the two unilateral ones were affected on the left. Only two were in male children. Every patient with cervical rib had a long neck and a hyposthenic thorax. A marked variation was noted in the size and contour of the anterior root of the transverse process of the seventh cervical vertebra. In many instances it reached such proportions that it was difficult to differentiate it from a rudimentary cervical rib. This may be explained by the developmental anatomy of the seventh cervical vertebra. The diagnosis of cervical rib will be made more frequently if the symptom complex is borne in mind. Oblique roentgenograms of the neck and the upper part of the chest taken with the rays directed upward, laterally and posteriorly through the seventh cervical vertebra will demonstrate more clearly the actual proportions of the rib. In the interpretation of roentgenograms of children less than 5 years of age, the presence of a separate piece of bone adjacent to the transverse process of the seventh cervical vertebra should be recognized as a center of ossification which is a potential precursor of a cervical rib.

**Poliomyelitis Following Tonsillectomy.**—Stillerman and Fischer studied the 686 patients with poliomyelitis who were admitted to the Willard Parker Hospital during 1935 in order to determine whether the removal of the tonsils and adenoids in any way influenced the onset or clinical type of the disease. It was found that tonsillectomy and adenoidectomy had been performed in ten cases during the month antedating the illness. In eight of these poliomyelitis began from ten to twelve days and in the other two sixteen and twenty-two days, respectively, after the operation. Six of the ten patients had the bulbar or encephalic form of the disease. Careful inquiry

was made among the fifty-two patients with poliomyelitis that were admitted to the hospital during 1937. In three of these patients tonsillectomy had been performed from two to three weeks preceding the onset of poliomyelitis. These three children had the bulbar type of disease. All of them died. The bulbar or encephalitic type of poliomyelitis was present in sixty-eight of the 686 patients and in fifteen of the fifty-two patients, while in six and three patients respectively who recently had their tonsils and adenoids removed the bulbar or encephalitic type developed. Thus there was a disproportionately high percentage of bulbar involvement in the tonsillectomized patients in both the 1935 and the 1937 outbreak. This much higher incidence of bulbo-encephalitic forms suggests the operative field as the port of entry of the virus. They conclude, therefore, that tonsillectomy and adenoidectomy should not be encouraged during an epidemic of poliomyelitis.

### Archives of Dermatology and Syphilology, Chicago

38: 511-678 (Oct.) 1938

- Contact and Environmental Allergens as Cause of Eczema in Infants and in Children. E. D. Osborne and H. L. Walker, Buffalo.—p. 511.  
Mycologic Technic for Study of Anascoporous Yeastlike Fungi. D. A. Berberian, Beirut, Syria.—p. 526.  
\*Liquefying Nodular Panniculitis: Report of Case. B. Shaffer, Philadelphia.—p. 535.  
Parapsoriasis en Plaques Disséminées and Incipient Mycosis Fungoides: Supplementary Data on Their Relationship. H. Keil, New York.—p. 545.  
Juvenile Pemphigus: Effects of Germanin in Three Cases. C. C. Tomlinson, with collaboration of O. J. Cameron, Omaha.—p. 555.  
Is Lichen Nitidus a Variety of Lichen Planus? F. A. Ellis, Baltimore, and W. F. Hill, Philadelphia.—p. 569.  
Melanotic Sarcoma with Extreme Melanosis: Report of Case. H. A. Dixon, Toronto.—p. 574.  
Psoriasis of Nails. G. M. Crawford, Boston.—p. 583.  
Serologic Paradox in Juvenile Dementia Paralytica: Report of Case. S. M. Bouton Jr., Ingleside, Neb.—p. 595.  
\*Treatment of Herpes Simplex with Moccasin Venom. R. J. Kelly, New York.—p. 599.  
Multinucleated (Giant) Cell Tumor of Gum (Epulis). W. Sachs, Jersey City, N. J., and W. Garbe, Toronto.—p. 603.  
Zosteriform Lichen Planus. M. I. Davis, Nashville, Tenn.—p. 615.

**Liquefying Nodular Panniculitis.**—Shaffer presents a case of nodules in the subcutaneous fatty tissue, associated with fever. The essential clinical features are that (1) deep-seated, painful and tender, woody nodules appeared in the subcutaneous fatty tissue, (2) they evolved in from seven to ten days into cystic masses containing from 1 to 4 ounces (30 to 120 cc.) of an oily or fatty yellowish brown fluid, (3) just before rupture (from ten to fourteen days) the skin overlying the mass was livid and raised while the central portion was attenuated into a thin translucent bulla-like membrane, (4) a deep cuplike depression formed in the subcutaneous fat, associated with a thin puckered scar, at the site of the healed lesion, (5) fever was present when the active lesions were most numerous and (6) the lesions occurred on the buttocks and extremities. The histologic features of the process are a primary round cell infiltration, the disappearance of the fat cells and their replacement by foam cells and the eventual liquefaction of the process.

### Treatment of Herpes Simplex with Moccasin Venom.

—Kelly treated fifteen cases of herpes simplex and three of herpes zoster with moccasin venom in a 1:3,000 dilution. The venom was given intradermally in doses of 0.2 cc. Since the disease is usually of short duration, an attempt was made to treat it only in the incipient stage, i. e. when itching, burning, swelling and slight vesiculation were present. In twelve cases of herpes simplex in which treatment was begun early, i. e. within eight to twenty-four hours after onset, the subjective symptoms disappeared within five to twelve hours after the snake venom was injected and the swelling and vesiculation disappeared within twelve to thirty-six hours, the vesicles being replaced by small dry crusts with no exudation. In the three other cases, in which the eruption had been present for longer than twenty-four hours, the duration and course of the disease were unaltered, although the patients stated that the subjective symptoms were noticeably lessened. The course of the disease in the three cases of herpes zoster appeared to be unaltered. However, the patients, each of whom had complained of severe burning and itching when first seen during the stage of vesiculation, stated that the subjective symptoms were alleviated.

### Iowa State Medical Society Journal, Des Moines

28: 473-524 (Oct.) 1938

- General Indications and Contraindications for Operative Delivery. E. D. Plass, Iowa City.—p. 473.  
General Consideration of Occipitoposterior Positions During Labor. L. E. Kelley, Des Moines.—p. 475.  
The Forceps Operation. H. A. Weis, Davenport.—p. 476.  
The Aftercoming Head. W. F. Mengert, Iowa City.—p. 478.  
The Cesarean Problem. E. D. Plass, Iowa City.—p. 481.  
Other Obstetric Operations. O. N. Glesne, Fort Dodge.—p. 483.  
Maternal Hazards of Operative Delivery. J. H. Randall, Iowa City.—p. 485.  
Hazards to the Fetus in Operative Deliveries. R. E. Crowder, Sioux City.—p. 487.

### Journal of Nutrition, Philadelphia

16: 309-406 (Oct.) 1938

- Production of Manganese Rickets in Rats. H. Blumberg, D. H. Shelling and Deborah A. Jackson, Baltimore.—p. 317.  
Spectrum Analysis for Trace Elements in Ashes of Human, Goat and Cow Milk. W. F. Drea, Colorado Springs, Colo.—p. 325.  
Excretion of Vitamin B<sub>1</sub> in Urine and Feces. R. F. Light, A. S. Schultz, L. Atkin and L. J. Cracas, New York.—p. 333.  
Study of Biophotometer as Means of Measuring Vitamin A Status of Human Adults. L. E. Bocher and D. E. Williams, Washington, D. C.—p. 343.  
Nicotinic Acid in Prevention of Blacktongue of Dogs. W. H. Schrell, R. H. Onstott, H. F. Fraser and F. S. Daft, Washington, D. C.—p. 355.  
Content of Reduced Ascorbic Acid in Blood Plasma in Infants, Especially at Birth and in the First Days of Life. P. W. Braestrup, Iowa City.—p. 363.  
Change in Total Energy Metabolism of Rats Receiving a Diet Deficient in Inorganic Constituents. M. Kriss and A. H. Smith, New Haven, Conn.—p. 375.  
Oxidative Changes Induced by Mineral Deficient Diet. M. Kriss and A. H. Smith, New Haven, Conn.—p. 385.  
Anomalies in Bio-Assay of Vitamin D Milk. K. Morgareidge and B. O'Brien, Rochester, N. Y.—p. 395.

### New Jersey Medical Society Journal, Trenton

35: 585-648 (Oct.) 1938

- \*Treatment of Myoma Uteri. T. B. Lee, Camden.—p. 590.  
Endogenous Infections of the Eye, Particularly Uveitis. C. H. Schlichter, Elizabeth.—p. 594.  
Treatment of Endogenous Infections of the Eye. E. S. Sherman, Newark.—p. 596.  
Buried Grafts Used to Repair Depressions in the Brow, Eye Socket, Skull and Nose. L. A. Peer, Newark.—p. 601.  
Water Balance from the Laboratory Point of View. J. W. Gray, Newark.—p. 606.  
Induction of Labor: Maternal Welfare Article Number Thirty. R. A. MacKenzie, Asbury Park.—p. 611.

**Treatment of Myoma Uteri.**—Lee states that of the last 3,000 cases admitted to the gynecologic service of the Cooper Hospital 500 have been cases of fibromyoma. Myomectomy was performed in twenty. This is the preferred method of treatment whenever possible. It has been most useful in pregnancy complicated by fibroid. Myomectomy should always be done in submucous fibroids in the nonpregnant young patients. The author considers extensive adnexitis, very large tumors and nearness to the approaching menopause contraindications to myomectomy. When indicated, the morbidity and mortality of myomectomy are negligible. Subtotal hysterectomy was performed in 385 cases. The mortality and morbidity of subtotal hysterectomy are low owing to the fact that the technic has been simplified and standardized in recent years. Total hysterectomy was done in five cases. The total operation is done when malignant manifestations in the cervix are suspected. In other cases the cervix, after receiving proper treatment, may safely remain. Amputation, tracheloplasty or the cautery may be used to accomplish this purpose, although tracheloplasty is preferred in the average case. In selected cases vaginal hysterectomy is undoubtedly a procedure of choice, with a low mortality and most gratifying convalescence. Its use should be restricted to those cases in which there has been no history of severe pelvic infections and in which neither the uterus nor the adnexa appear fixed by adhesions. Total vaginal hysterectomy is indicated for very stout persons, for old persons with a small tumor, for patients who have no history of severe pelvic inflammation, in procidentia when removal of the uterus is desirable and in suspicious conditions of the cervix with fibromyoma with a roomy pelvis. Vaginal hysterectomy for the removal of large fibroids is to be deplored. When radium is used the tumor should not be larger than a three months pregnancy, it

should not be pedunculated, there should be no pressure-symptoms on the bladder or the intestine, there should be no history of recent pelvic inflammation and the patient should be at or near the menopause or older. Radium was used in fifty-four cases of the present series. The symptom for which radium has been used is uterine bleeding and no reirradiation has been necessary. The reduction in the size of the tumor averages about one third and requires about one year to be complete. X-ray irradiation has little place in the treatment of fibroids. It should be reserved for inoperable cases, cardiac or otherwise and in some tumors too large for radium. Small fibroids which do not give rise to symptoms should be left alone. Many of these grow slowly and never attain sufficient size to menace the patient's health. They practically all tend to retrogress at the menopause. A malignant growth in the fundus was encountered in four of the 500 patients. Five patients died, one each from hemorrhage, septicemia, coronary thrombosis, peritonitis (complicating cancer of the rectum) and diabetes.

### Pennsylvania Medical Journal, Harrisburg

42: 1-96 (Oct.) 1938

- Serum Therapy of Pneumococcic Pneumonias. J. G. M. Bullowa, New York.—p. 17.  
Functions of the Special Examining Boards. P. Titus, Pittsburgh.—p. 22.  
Sight-Saving Classes. M. E. Smukler, Philadelphia.—p. 24.  
Simmonds' Disease: Case Report. C. Rea and P. A. Hoover, York.—p. 27.  
Psychology in Medicine. J. A. Cammarata, Danville.—p. 31.  
\*Dyspnea in Anthracosilicosis: Clinicopathologic Study. R. Charr and J. W. Savacool, White Haven.—p. 35.  
The Organization and Function of a Physical Therapy Department in a General Hospital. B. S. Troedsson, Bryn Mawr.—p. 39.  
Backache in Women. J. B. Raddin, Hazleton.—p. 43.  
Diagnosis and Treatment of Anorectal Fistulas. H. E. Bacon, Philadelphia.—p. 45.  
Injection Treatment for Varicose Veins in Lower Abdomen. E. F. McLaughlin, Philadelphia.—p. 51.  
Return of Electrocardiogram to Normal in Coronary Thrombosis with Nine-Lead Serial Electrocardiographic Studies. V. A. Digilio, J. A. Pescatore and J. B. Wolfe, Philadelphia.—p. 53.  
Undulant Fever: Report of Treatment of Three Cases with Mixed Typhoid Vaccine Intravenously. L. E. Etter, Warrendale.—p. 58.  
Hemolytic Jaundice: Report of Case. W. C. Hendricks, Brookville.—p. 61.  
Insulin Hypoglycemia in Schizophrenia. R. W. Staley, Pittsburgh.—p. 63.

**Dyspnea in Anthracosilicosis.**—Charr and Savacool determined the vital capacity, venous pressure and pulmonary circulation in twenty cases of pure anthracosilicosis and for comparison twenty cases of tuberculosis in which there was marked collapse of one lung under artificial pneumothorax or thoracoplasty. They found that dyspnea in anthracosilicosis is not always directly proportional to the reduction of the vital capacity while it is to the length of the pulmonary circulation time. In fact it appears that this dyspnea is largely due to cardiac insufficiency. Myocardial degeneration is a common observation in anthracosilicosis and is due to pulmonary fibrosis, emphysema and pulmonary arteriosclerosis, which are almost always present. When an anthracosilicotic patient is studied for compensation, possible myocardial insufficiency as well as the pulmonary damage should be determined. For such study the estimation of the velocity of the pulmonary circulation may give aid.

### Public Health Reports, Washington, D. C.

53: 1733-1774 (Sept. 30) 1938

- Mottled Enamel Survey of Bauxite, Ark., Ten Years After a Change in the Common Water Supply. H. T. Dean, F. S. McKay and E. Elvove.—p. 1736.

53: 1775-1816 (Oct. 7) 1938

- \*Report of Two Cases of Rocky Mountain Spotted Fever in Ohio. M. L. Cooper, M. A. Kurzner, Armine T. Wilson and R. E. Dyer.—p. 1775.  
Simple Method of Concentrating Vitamin E. C. G. Mackenzie, Julia B. Mackenzie and E. V. McCollum.—p. 1779.

**Rocky Mountain Spotted Fever in Ohio.**—Cooper and his associates report the histories of two patients who were bitten by ticks and who later had extensive generalized macular-papular-petechial rashes which also involved the palms in both patients and the soles in one. Both patients showed definite Weil-Felix agglutination reactions. One patient died. A strain isolated from the patient who died was proved to be Rocky Mountain spotted fever by studies in laboratory animals.

### Rocky Mountain Medical Journal, Denver

35: 745-832 (Oct.) 1938

- Useful Hints in Diagnosis and Treatment of Gastrointestinal Disease. W. C. Alvarez, Rochester, Minn.—p. 770.  
Alar Scapula. P. M. Schunk, Sheridan, Wyo.—p. 776.  
Sterile Obstetric Package. Ruth E. Phillips, Denver.—p. 778.  
\*The Need for Prolonged Sulfanilamide Therapy in Certain Infections. G. R. Alpert, New York, and R. P. Forbes, Denver.—p. 779.  
Sulfanilamide Therapy in Otolaryngology. H. L. Hickey, Denver.—p. 782.

**Prolonged Use of Sulfanilamide.**—Alpert and Forbes contend that severe streptococcal and meningococcal infections, such as otitis, cervical adenitis, sinusitis, mastoiditis and involvement of the meninges, demand intensive and prolonged administration of sulfanilamide if relapses are to be obviated. In a series of 200 children given sulfanilamide therapy by one of the authors relapses occurred in approximately 7 per cent. Otitis and cervical adenitis were the most frequent complications tending to relapse and required prolonged administration of sulfanilamide. Impetigo contagiosa yields promptly to sulfanilamide, but relapses are not infrequent following courses of from three to five days of the drug. Severe toxic effects of sulfanilamide can be avoided if the leukocyte count, the hemoglobin percentage and the concentration of sulfanilamide in the blood are determined daily for patients receiving large doses of the drug. The rationale for continuous treatment can be found in the mode of action of the drug. It is now generally agreed that the action of sulfanilamide is mainly that of bacteriostasis and not that of a bactericide.

### South Carolina Medical Assn. Journal, Greenville

34: 251-278 (Oct.) 1938

- Acute Perforation of Gastric and Duodenal Ulcers. G. H. Bunich, Columbia.—p. 251.  
Congenital Narrowing of the Ileum: Report of Case. G. D. Johnson, Charleston.—p. 256.

### Southern Medical Journal, Birmingham, Ala.

31: 1043-1116 (Oct.) 1938

- Diverticulum of the Female Urethra. H. H. Young, Baltimore.—p. 1043.  
Plastic Surgery of the Nose: Report of an Original Operation for Advancement of Nasolabial Fold. B. Douglas, Nashville, Tenn.—p. 1047.  
Treatment of Malignancy with Small Radium Needles Combined with X-Ray. R. H. Crockett, San Antonio, Texas.—p. 1053.  
Aminopyrine Treatment of Rheumatic Endocarditis Associated with Active Rheumatic Infection: Preliminary Report. B. R. Heninger and G. McHardy, New Orleans.—p. 1056.  
The Place of Diuretics in Congestive Heart Failure. R. Lyons, New Orleans.—p. 1059.  
Chronic Brucellosis of Twenty-Five Months' Duration: Report of Case with Necropsy Findings. E. E. Menefee and Mary A. Poston, Durham, N. C.—p. 1061.  
\*Encephalomyelitis Complicating the Virus Infections: Report of Seven Cases. F. H. Lancaster, Houston, Texas.—p. 1063.  
The Artificial Pneumothorax. M. W. Miller, New Orleans.—p. 1072.  
Clinical Aspects of Gastric Hemorrhage. S. M. Copland, New Orleans.—p. 1075.  
Medical Aspects of Carcinoma of the Colon, with Special Reference to the Early Diagnosis. J. Friedenwald and M. Feldman, Baltimore.—p. 1078.  
The Terminal Ileum: Its Surgical Importance with Special Consideration of Selected Lesions. A. H. Storck, New Orleans.—p. 1087.  
Prolapse Through the Anal Sphincters. R. L. Murdoch, Oklahoma City.—p. 1091.  
Unusual Complication of Radical Antrum Operation. T. E. Fuller, Texarkana, Texas.—p. 1094.  
Athetosis: Surgical Treatment: Preliminary Report of Four Cases, Three Unilateral and One Bilateral. R. M. Klemme, St. Louis.—p. 1095.  
Technic for Wiring Aortic Aneurysms. R. M. Penick Jr., New Orleans.—p. 1096.  
Subacromial Bursitis. J. D. Collins, Norfolk, Va.—p. 1098.  
Dust: Its Effect on Man from a Medical Standpoint, with Special Reference to the Dust Bowl. J. A. Blue, Guymon, Okla.—p. 1101.  
Use of Social Security Funds in Expansion of the Louisiana Public Health Program. R. W. Todd, New Orleans.—p. 1106.

**Encephalomyelitis Complicating Virus Infections.**—Lancaster reports seven cases of encephalomyelitis in which the etiologic factor is considered to be a filtrable virus. Three followed chickenpox, two measles, one vaccination and one mumps. Encephalomyelitis complicating any of the virus infections may show a wide variation in symptoms, but in chickenpox the particular points that stand out are (1) the infrequency of headache as a symptom, (2) a marked tendency to cerebellar disturbance and (3) favorable prognosis, both as to life and as to the absence of sequelae. Since there is a definite associa-

tion between vaccination and the consequent encephalomyelitis there can be little doubt that vaccination is etiologic, although such complications are rare. In most cases the period elapsing between the time of vaccination and the onset of nervous symptoms is fairly constant (ten days). Sequelae have been rare: the principal distinguishing point between this condition and epidemic encephalitis. In measles the prominent features are (1) the greater tendency to polymorphism of symptoms and (2) the extremely high percentage of cases showing definite and permanent damage to the nervous system. In measles as well as in the other conditions the severity of the primary illness is not a determining factor in the occurrence of complications or the severity of the complications when they appear. In mumps probably the most common complication is that of meningeal irritation, and the symptoms follow closely those of true meningitis. In the case reported the noteworthy feature was the myelitis, which comes under the rarer forms of neurologic complications in this disease. The prognosis is favorable with an exceptionally low mortality and a tendency to a complete recovery and in those cases showing only meningeal symptoms the course of the illness is brief.

### Southwestern Medicine, El Paso, Texas

22: 391-428 (Oct.) 1938

- Surgical Shock. D. L. Secrist, Tucson, Ariz.—p. 391.  
Management of Bowel Obstruction. D. F. Monaco, Gallup, N. M.—p. 393.  
Subinvolution of the Uterus. G. Heusinkveld, Denver.—p. 397.  
Ectopic Pregnancy. L. M. Miles, Albuquerque, N. M.—p. 401.  
Fractures of Forearm and Lower Leg. L. W. Breck, El Paso, Texas, and C. Basom, Rochester, Minn.—p. 404.  
Lead Absorption and Lead Poisoning: H. J. Rogde, El Paso, Texas.—p. 407.

### Surgery, Gynecology and Obstetrics, Chicago

67: 413-576 (Oct.) 1938

- \*Alternation of Blood Supply as Cause for Normal Calcification of Bone. H. C. Blair, Portland, Ore.—p. 413.  
Salivary Gland Tumors. N. W. Swinton and S. Warren, Boston.—p. 424.  
Acute Safety of Ether, Divinyl Ether and Chloroform in Production of "Obstetric Degree" of Analgesia. W. B. Draper and R. W. Whitehead, Denver.—p. 436.  
Swollen Atrophic Hand. A. Oppenheimer, Beirut, Syria.—p. 446.  
Normal and Pathologic Developments from Cells Lining Graafian Follicle. W. S. Gardner, Baltimore.—p. 455.  
Scoliosis. S. Kleinberg, New York.—p. 467.  
Renal Function Tests in Differentiation of Bright's Disease from So-Called Specific Toxemia of Pregnancy. L. C. Chesley, Jersey City, N. J.—p. 481.  
Blood Volume and Hemoglobin After Transfusion. W. L. Sibley and J. S. Lundy, Rochester, Minn.—p. 490.  
Technic of Gastroduodenectomy. C. A. Pannett, London, England.—p. 495.  
\*Radical Treatment of Intractable Pruritus Ani. S. D. Manheim and L. J. Druckerman, New York.—p. 500.  
Carcinoma of Major Vestibular (Bartholin) Gland. S. M. Rabson and L. H. Meeker, New York.—p. 505.  
Technic for Transfusion of Blood into Abdominal Aorta. E. B. Tuohy, Rochester, Minn.—p. 510.  
Carcinoma of Rectum and Rectosigmoid: Ligation of Internal Iliac Arteries. H. B. Keyes, New York.—p. 512.  
Modified Well Leg Traction Splint and Distractor Combined. C. H. Watt, Thomasville, Ga.—p. 515.  
Aberrant Pancreatic Tissue in Gastrointestinal Tract: Report of Two Cases and Review of Literature. M. Danzis, Newark, N. J.—p. 520.  
Reliable Control for Steam Sterilization. C. W. Walter, Boston.—p. 526.

**Blood Supply and Calcification of Bone.**—Blair states that disuse is known to produce rarefaction and bone atrophy. This rarefaction is due to the absorption of the mineral elements of bone. The cellular constituents remain and as activity is resumed the complicated bone salt is replaced. Activity is due to one thing only—the contraction and relaxation of muscles controlling the extremity involved. Ischemia, even slight, will produce a localized acidosis in the pressure area. The change toward the acid reaction and toward the alkaline side appears to be accomplished quickly and by very little change in the blood supply. By the contraction and relaxation of muscles it would seem that these changes could be brought about in bone. It does not seem possible that reossification of bone is produced in any other way; weight bearing and stress and strain can be ruled out because even the slight activity of a person confined in bed will prevent the atrophy of the bone or bones of a limb not encased in plaster. Alternating ischemia and hyperemia can

produce a comparative alternation in the hydrogen ion content of tissue fluids. It is assumed that during a rest period when muscles are relaxed, particularly just after exercise, when arterial flow is markedly increased, a swing toward the alkali side is taking place. Phosphatase acts best in hydrolysis of the phosphoric ester in an alkaline medium. At this period inorganic phosphates should increase in the tissue fluids. Muscular contraction taking place produces an ischemia, a lower hydrogen ion concentration, and as a more acid reaction develops more calcium is ionized and the tissue fluids are able to hold in solution a higher supersaturation of calcium. As muscular relaxation takes place and the swing is again toward a higher hydrogen ion concentration, the law governing salts that are soluble with difficulty causes a precipitation of the complex bone salt, composed of calcium carbonate and calcium phosphate. Theoretically it would seem that the clinical use of alternating suction and pressure, by increasing and diminishing the blood supply to the part by contraction and relaxation of the muscles, might aid in the production of union.

**Treatment of Intractable Pruritus Ani.**—Manheim and Druckerman excised completely all the diseased tissues in three cases of severe and intractable pruritus ani accompanied by advanced cutaneous changes. The operation is as follows: The sphincter is gently dilated, not divulsed. The entire affected area is circumscribed by a circular incision, which usually is at a radial distance of from 2 to 3 inches from the anal margin. The incision is carried down through the entire thickness of the skin until normal subcutaneous fat is encountered. The dissection is then continued in the subcutaneous tissue up to the mucocutaneous junction. The fibers of the corrugator cutis ani muscles are severed, and the subcutaneous portion of the external sphincter muscle is carefully exposed and protected. The cone shaped area of the skin is then split anteriorly and posteriorly in order to facilitate the subsequent section at the mucocutaneous junction, which is performed after clamps are placed on the mucous membrane to prevent retraction. The gluteal skin is mobilized for a distance of from 1 to 2 inches. All bleeding points are carefully controlled. Four silk mattress sutures are placed between the mucous membrane and the cutaneous edges at equidistant points anteriorly, posteriorly and laterally. Interrupted silk sutures are used to complete the approximation. A small piece of petrolatum gauze is inserted into the newly constructed anal canal and the entire operative area is covered with it. The results were gratifying. Pruritus disappeared immediately after operation. Surprisingly little pain was present throughout the convalescence. Complete healing occurred in from six to ten weeks. All three patients have been completely relieved and have remained so for from four to twenty-two months after operation. The method is not recommended for the treatment of the usual case of pruritus ani but only for long standing, intractable pruritus ani, particularly when accompanied by pronounced and possibly premalignant cutaneous changes.

### Virginia Medical Monthly, Richmond

65: 583-650 (Oct.) 1938

- Incidence and Importance of Human Intestinal Parasites in Tidewater, Virginia. W. B. Martin, Norfolk.—p. 585.  
Undesirable Effects Following Use of Sulfanilamide. C. C. Haskell, Richmond.—p. 587.  
Diagnosis and Treatment of Acute Head Injuries. J. M. Meredith, University.—p. 591.  
Epididymitis. J. A. Grendeske and W. M. Brunet, Chicago.—p. 598.  
Etiology of Malignant Tumors. C. Williams, Richmond.—p. 602.  
Psychologic Conditioning. P. G. Hamlin, Cambridge, Md.—p. 605.  
Present Preventive Programs for Feeble-minded and Mentally Ill People in Virginia. J. N. Williams, Richmond.—p. 609.  
Problems of the Rural Physician of Yesteryear. L. Holladay, Orange.—p. 611.  
Carbuncle of the Kidney. R. L. Ozlin, New York.—p. 614.  
Anorectal Stricture of Lymphopathia Venerica. J. Parrish, Portsmouth.—p. 617.  
Pyelitis: Etiology and Pathology. W. F. Burdick, Washington, D. C.—p. 621.  
Id.: Symptoms, Diagnosis, Treatment. J. M. Moser, Washington, D. C.—p. 622.  
Sulfanilamide: Its Uses and Dangers. F. M. Howell, Hopewell.—p. 625.  
Serum Treatment of Pneumonia. C. P. Jones Jr., Newport News.—p. 628.  
Treatment of Abortion. R. von Lehn Buxton, Newport News.—p. 632.  
Socialized Medicine. J. E. Rawls, Suffolk.—p. 635.

## FOREIGN

An asterisk (\*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

## British Medical Journal, London

2: 691-728 (Oct. 1) 1938

- Acute Appendicitis. G. G. Turner.—p. 691.  
Carbohydrate Metabolism in Anesthesia: Review. R. R. Macintosh and C. L. G. Pratt.—p. 695.  
\*Use of Bacteriophage in an Outbreak of Institutional Dysentery. D. Haler.—p. 698.  
Observations on Potency and Stability of Dick Test Toxins. H. M. Leete, J. McGarrity, F. L. Ker and J. Reid.—p. 700.  
Note on Diphtheria Immunization in London. M. Sorsby.—p. 701.  
Vasomotor Rhinorrhea, with Asthma, Associated with Menstruation. A. S. Hoseason.—p. 703.

**Bacteriophage in Dysentery.**—Haler discusses an outbreak of dysentery in an institution for blind children (population thirty-two) from a few months to 7 years of age. The first patient became ill Feb. 20, 1937. The only important symptom was a little blood in the stools. This child was not suspected of having dysentery and after being segregated for a few days was allowed to join the other children freely. The epidemic followed six weeks later, but April 22 the same child was ill again. On the latter occasion the first stool to be examined showed no dysentery bacilli, but April 25 *Bacillus dysenteriae* Sonne was obtained. Following this presumed first case of February 20 there were three cases on April 4 and 5, four more cases April 10 and 11, another febrile case of dysentery occurred April 18, and April 22 the first patient was again reported ill. It is possible that this patient may have harbored *Bacillus sonnei* from February 20 and thus have been the source of the other infections. April 25, three more cases occurred. Bacteriophage treatment was recommended for those who had been sick, those unaffected and all the staff. All those in bed and on bed isolation received dysentery bacteriophage three times daily until the stools were reported "free from *Bacillus dysenteriae* Sonne and from atypical dysentery bacilli." On the second day after treatment was begun, one further case occurred. This was the last; and now, more than a year later, there has been no fresh case. This sudden cessation of the epidemic may have been a coincidence, but there was nothing to suggest that the cases between April 4 and 27 were being infected from outside the home. The repeated isolation of *Bacillus dysenteriae* Sonne from the stools suggested that this infection was being spread. No medicinal treatment other than bacteriophage was administered.

## Journal of Hygiene, London

38: 521-646 (Sept.) 1938

- Leptospiiral Infections in Rats: Presence of Specific Leptospiiral Immune Bodies in Serum and Their Relationship to Carrier Conditions. J. Smith.—p. 521.  
Bacterial Content of Ice Cream in Relation to Manufacture, Storage and Standards of Purity. Doris A. Bardsley.—p. 527.  
Further Observations on Influence of Growing Family on Diet in Rural Districts in Sussex. F. Brockington.—p. 547.  
Some Observations on Rideal-Walker Test. A. C. Thaysen.—p. 558.  
Investigation of Normal Agglutinins for Typhoid and Paratyphoid Bacilli in Human Serums in Victoria and Interpretation of Widal Test. T. S. Gregory and Nancy Atkinson.—p. 566.  
Mortality of Hemolytic *Streptococcus* on Skin and on Other Surfaces. J. M. L. Burtenshaw.—p. 575.  
\*Growth of *Salmonella* Typhi and Certain Other Members of *Salmonella* Group in Milk and Butter Stored at Atmospheric Temperatures. E. J. Pullinger and Audrey E. Kemp.—p. 587.  
Study of English Diets by Individual Method: III. Pregnant Women at Different Economic Levels. R. A. McCance, E. M. Widdowson and C. M. Verdon-Roe.—p. 596.  
Experiments on Staphylococcal Food Poisoning. F. C. Minett.—p. 623.  
Adsorbent Effects of Various Dusts on Diluted "Old Tuberculin." S. L. Cummins and Enid M. Williams.—p. 638.

**Salmonella in Milk and Butter.**—The experimental results of Pullinger and Kemp show that the *Salmonella* which is likely to contaminate milk supplies and which causes either typhoid or food poisoning in man grows readily in freshly drawn milk stored under normal commercial or household conditions when refrigeration is not resorted to. Any effect exerted by the growth-inhibitory factor of fresh milk is transient, since multiplication was observed even after small initial inoculums had been added to the milk. The inhibitory factor was not bactericidal for *Salmonella*. Whether contamination originates

from the cow, as usually happens with *Salmonella dublin*, or from some external source as with *Salmonella typhi*, the really important factor in the epidemiology of milk borne *Salmonella* outbreaks is that the contaminating organism can thrive during storage and thus cause wholesale contamination of pooled milk. A point of some interest which has arisen out of the investigation is the fact that strains of *Salmonella typhi* recently isolated from human cases multiplied more rapidly in milk than did old laboratory stock cultures. When artificially incorporated in butter after manufacture, these organisms were found to survive for periods varying from two to three months and even longer when the butter was stored at 15 or 3 C. Neither the quality of the butter nor the presence or absence of salt appeared to influence this survival. There was no suggestion that any multiplication occurred, and after about two months' storage the organisms began to decrease in numbers.

## Journal of Physiology, London

93: 305-438 (Sept. 16) 1938

- Relation of Contracture to Increment in Resting Heat Production of Muscle Under Influence of Potassium. C. G. Smith and D. Y. Solandt.—p. 305.  
Synchronized Impulse Discharges from Receptors in Deep Tissues in Response to Vibrating Stimulus. F. Echlin and A. Fessard.—p. 312.  
Absorption of Ultraviolet Radiation by Human Sweat. W. H. Crew and C. H. Whittle.—p. 335.  
Phase Angle of Normal Human Skin. A. Barnett.—p. 349.  
Study of Source of Liver Fat Using Deuterium as an Indicator. H. M. Barrett, C. H. Best and Jessie H. Ridout.—p. 367.  
Accuracy of Thermotromuhr Method for Measuring Blood Flow. H. Barcroft and W. M. Loughridge.—p. 382.  
Experiments on Relation Between Thyroid Gland and Lactation in the Rat. S. J. Folley.—p. 401.  
Maximal Growth Rate of Capon Comb. C. W. Emmens.—p. 413.  
Some Effects of Compounds of Androsterone-Testosterone Series on Ovariectomized Mice. C. W. Emmens.—p. 416.  
Effect of Subarachnoid Administration of Histamine on Rate of Absorption of Isotonic Saline Solution in the Dog. T. H. B. Bedford.—p. 423.  
Effect of Hypertonic Solutions on Gastric Secretion and Intra-Ocular Pressure. R. L. Noble and J. D. Robertson.—p. 430.

## Lancet, London

2: 761-812 (Oct. 1) 1938

- The Heart Sounds in Normal and Pathologic Conditions. E. Braun-Menendez.—p. 761.  
Duration of Action of Zinc Protamine Insulin. R. S. Aitken.—p. 768.  
\*Air Embolism: Reports of Three Cases. G. R. Osborn and J. C. C. Dawson.—p. 770.  
Carcinoma of the Tongue: Late Results of Treatment. R. Phillips.—p. 772.  
Osteomalacia of Spine Following Abuse of Laxatives. E. Meulengracht.—p. 774.

**Air Embolism.**—Osborn and Dawson report three cases of air embolism: two complicating labor at full term free from infection (in each the postmortem examination was made before decomposition could complicate the observations) and one of a boy aged 16. None had been treated with chemicals. At necropsy both women showed definite fatty changes in the liver, a condition often found in unexpected deaths. In the first case the severity of this change may have been the reason for the extraordinary atonicity of the uterine muscle. The histories of the two women from the time the air presumably gained access to the veins is strikingly similar and the times taken to die (three and one and one-half hours) are noteworthy. The liver and alimentary tract in the third case appeared normal. The kidneys showed a severe chronic nephritis which was evidently responsible for the cardiac hypertrophy. The renal pelvis and ureters were normal. The bladder was empty; there was a hemorrhage of about 60 cc. into the tissues to the left of it, which was not connected with the much larger hemorrhage into the mediastinal tissues. There was no tear of the bladder or injury of the rectum. According to the mother, the boy seemed all right when he got out of bed to pass urine, so that much of the blood present in the pleural cavity was probably the result of postmortem bleeding. Air embolism presents characteristic symptoms. These are sudden onset, disappearance of the pulse, deep respirations with air hunger, restlessness with chest discomfort (shown especially by lashing about with the arms) pallor if the case is immediately fatal, associated with fright and cyanosis if death is delayed. If the condition should be recognized during life it is conceivable that aspiration of the right side of the heart would avert a fatal issue.



**Journal de Médecine de Lyon**

19: 527-554 (Sept. 20) 1938

\*Etiology of Angina Pectoris. L. Gallavardin.—p. 527.

**Etiology of Angina Pectoris.**—The anginal syndromes which are the object of this study by Gallavardin are those of true angina of coronary origin. This statistical report, which is based on approximately 1,900 cases, reveals that angina pectoris is much more frequent in men than in women, the ratio being about 4:1. The onset of the anginal symptoms is most frequent in persons between the ages of 45 and 65 years; that is, in nearly 75 per cent of the cases the onset occurs during those years. The role of syphilis is important but limited and the author thinks that formerly the significance of syphilis in angina pectoris was greatly exaggerated. The proportion of syphilitic patients (certain and doubtful cases) does not exceed 20 per cent of the total number of patients with angina pectoris. However, the influence of this infection is the more evident, the younger the patients are; it plays a part in not far from 50 per cent of those under 35, in nearly 40 per cent of those under 40 and in nearly 25 per cent of those under 50. In those above the age of 50 the incidence decreases rapidly to from 15 to 18 per cent for men and to from 5 to 8 per cent for women. The author says that nicotine is not the only cause of nonsyphilitic angina pectoris. Of the men with nonsyphilitic angina pectoris, more than 20 per cent had never smoked; if the women are included, the percentage of nonsmokers exceeds 40. Coronary angina pectoris by itself has nothing in common with arterial hypertension. In the author's material more than 60 per cent of the men had a tension which did not exceed 160 mm. of mercury. However, the coexistence of the two disorders is quite common in women as well as in men. It is even possible that certain hypertensive states provoke, especially in women, the appearance of an anginal syndrome which does not depend on coronary lesions.

**Presse Médicale, Paris**

46: 1449-1464 (Oct. 1) 1938

\*Buccal Cacosmias. G. Sanarelli.—p. 1449.

Hemorrhagic Rectitis. P. Oury and R. Stieffel.—p. 1452.

**Buccal Cacosmias.**—Sanarelli says that halitosis, or buccal cacosmia, has nothing in common with the enteropulmonary gaseous exchange, by which the odors of certain ingested substances may be temporarily noticeable in the expired air. Buccal cacosmia is not a transitory condition but a permanent disorder, which frequently exerts a harmful influence on the psyche of the patient. Medical science has ascribed it to banal causes such as digestive irregularities or poor condition of the teeth. The buccal cacosmia with which the author is concerned in this report is of the "essential" type, which should not be confused with the halitosis of persons who have acute or chronic inflammatory processes with a pulmonary or buccopharyngeal localization such as pulmonary abscess, bronchiectasis, sinusitis, mercurial stomatitis, chronic tonsillitis or dental pyorrhea. He applies the term essential buccal cacosmia to the permanent halitosis in persons who otherwise appear healthy. Reviewing the hypotheses on the origin and nature of essential buccal cacosmia, he mentions those of Boldyreff and of Tamches. He directs attention to the antimicrobial action of saliva, which he demonstrated as early as 1892 and which was confirmed by other investigators. Further he describes his more recent studies on the bacterial flora, directing especial attention to the antiputrefactive action of the buccal streptococci. After describing several of his experiments on the bacterial origin of essential buccal cacosmia, he says that the results are always the same; that is, the buccal streptococci in the presence of even small quantities of carbohydrates succeed always by means of their acidifying diastases to impede the development (in the buccal cavity as well as in vitro) of other species of micro-organisms, including the putrefactive ones. If carbohydrates are lacking, the bacteria of putrefaction become predominant and in the presence of proteinic substances give rise to fetid odors. In the further discussion the author points out that, owing to the mild antimicrobial action

of the saliva, the continuous salivary irrigation of the buccal mucosa tends to reduce the abundant development of the oral bacterial flora. However, if the buccal or intestinal secretions undergo changes, the conditions become favorable for a free and abundant development of the bacterial flora. The author thinks that this is the reason why patients with disturbances of the digestive tract, who lack appetite and are nauseated, often have a fetid breath. These are the pathologic conditions of the stomach which exercise an indirect influence on the buccal mucosa and consequently on the salivary secretions. In the conclusion the author emphasizes once more that the origin of buccal cacosmia is not gastric, intestinal, pulmonary or due to particular microbes giving off the fetid odors. It is entirely local, being caused by banal putrefactive fermentations, which manifest themselves in the buccal cavity under the aforementioned abnormal local or general conditions.

**Revue Belge des Sciences Médicales, Louvain**

10: 341-392 (June-July) 1938

\*Clinical and Biologic Study of Pleural Effusion in Patients with Cirrhosis. M. Goffart.—p. 341.

Physicochemical Modifications of Blood After Surgical Interventions Under Various Anesthetics. I. Blitstein.—p. 371.

**Pleural Effusion in Patients with Cirrhosis.**—Goffart reviews the clinical histories of ten cases of pleural effusion in cirrhosis and then gives his attention to the pathogenesis. In conclusion he states that the pleural effusions are frequent in patients with cirrhosis. The appearance and evolution of pleural effusion is hardly noticeable and it must be searched for carefully in the course of the examination. The physical signs are deceiving, the roentgenologic examination underestimates the quantity of liquid and an exploratory puncture is necessary to settle the doubt. The pleural effusion does not aggravate the prognosis, except for septic complications. The effused fluid is relatively poor in albumin, fibrin and cholesterol. Its cytology is mixed; it always contains blood and the chloride content is increased. The pathogenesis is complex and it is unquestionably justifiable to invoke the mechanical causes of pulmonary stasis by elevation of the diaphragm; the reduction of the osmotic power of the proteins by inversion of the albumin/globulin ratio of the serum, and the impaired functional activity of the capillaries. The author says further that tuberculosis must still be regarded as a possible causal factor of pleurisy, but he did not detect it as a cause in the cases which he observed.

**Schweizerische medizinische Wochenschrift, Basel**

68: 1133-1152 (Oct. 8) 1938

Hemorrhagic Pleurisy in Children. Taillens.—p. 1133.

Pathogenesis and Therapy of Rheumatism. C. Haflter.—p. 1134.

Gold Therapy in Chronic Articular Rheumatism. W. Tschopp.—p. 1136.

Diagnosis of Adnextuberculosis. E. Held.—p. 1139.

\*Experimental Transmission of Poliomyelitis to Cattle. E. Frauchiger and W. Hofmann.—p. 1140.

**Experimental Transmission of Poliomyelitis to Cattle.**—Frauchiger and Hofmann cite Frauchiger's report about a case of spontaneous poliomyelitis in a heifer (THE JOURNAL, July 2, 1938, p. 74). This observation induced them to attempt the transmission of poliomyelitis to cattle, although it was generally believed that monkeys were the only animals that could be inoculated with this disease. Poliomyelitis material from human subjects (brain and spinal cord) was inoculated into three heifers aged between 12 and 18 months. Since it was the first aim to determine whether the inoculation would take, large doses were given and the material was introduced by three different routes (intranasal, intraperitoneal and intraspinal). Only one of the animals was not subjected to the intraspinal administration. Besides increases in temperature at the onset, there were no general symptoms such as gastrointestinal disturbances, nasal discharge and sweating. Moreover, there were no signs of meningeal irritation (stiffness of the back). However, after two or three days signs of paralysis appeared on the extremities, particularly the posterior ones. The paralytic symptoms increased to the seventh day. In one of the animals they persisted in about the same intensity, whereas in another one they disappeared, but never completely.

During the severest stage of the disease the animals had an atactic walk and frequently fell down. Completely flaccid paralysis was not observed. The third animal, which had not been subjected to intraspinal inoculation, showed a mild paresis which soon disappeared again. The walk and the behavior of the animals were recorded on a kinematographic film. In the fourth week after the inoculation, bilateral atrophy of the gluteal musculature was observed in one of the animals. In another animal atrophies were observed in the musculature of the pelvis and thighs as well as on the right foreleg. Examination of the cerebrospinal fluid of the animals revealed changes indicative of organic disease of the central nervous system, but since microscopic studies have not been made as yet the authors are unable to state whether the disease process is identical with that of poliomyelitis. However, further investigations will be devoted to such microscopic studies and to attempts to transmit the disease further by means of material obtained from these animals.

### **Annali di Ostetricia e Ginecologia, Milan**

60: 863-1007 (Aug. 31) 1938. Partial Index

Diagnosis of Malformation of Uterus by Metrography. E. Bortini.—p. 863.

Clinical Study of Treatment of Some Gynecologic Diseases by Androgen (Testosterone Propionate). A. Migliavacca.—p. 943.

\*Treatment of Puerperal and Postoperative Thrombosis and Thrombophlebitis of Legs. C. Pardella.—p. 973.

Kustallow's Reaction on Infusoria in Biologic Diagnosis of Normal and Ectopic Pregnancy. V. Pugliatti.—p. 991.

#### **Treatment of Thrombosis and Thrombophlebitis.**

Pardella reports satisfactory results of hirudinization (local application of leeches) and application of a bandage of wide adhesive tape in twelve cases of puerperal and postoperative thrombosis and thrombophlebitis of the legs. The leg is raised to about 40 degrees for a few minutes, during which the joints of the ankle and knee are covered with a thin layer of cotton and the bandage is applied from the distal end of the middle third of the foot up to a point near the root of the thigh. Compression and tension of the bandage are moderate and uniform. The toes are not included in the bandage, which is applied in such a manner that the lower half of each new turn of the adhesive tape covers the upper half of the turn previously applied. Immediately after application of the bandage, the patient is asked to perform a few slight movements of flexion and extension and the limb is placed at rest. Four or six leeches are placed at the anterolateral aspect of the thigh near its root. They are changed two or three times at intervals of twenty-four hours in septic thrombophlebitis and discontinued after the first application of twenty-four hours in simple thrombosis. A few moments are spent in flexion and extension on the sixth and ninth days of application of the bandage. According to the author the immobilization of the local venous system induced by the bandage results in normalization of the local venous and lymphatic circulations with consequent reabsorption of edema, improvement of the nutritional conditions of the tissues and rapid control of the disease. The patients are relieved from the first day. The treatment lasts for from nine to thirteen days, according to the evolution of edema, pain and the general symptoms. The satisfactory results are permanent, as verified by the author through further observation of the patients.

### **Giornale Veneto di Scienze Mediche, Venice**

12: 421-484 (Aug.) 1938. Partial Index

\*Residual Pain After Appendectomy: Surgical Intervention. G. Pieri.—p. 421.

Subcutaneous Traumatic Rupture of Common Tendon of Brachial Biceps Muscle. M. Tommasini.—p. 431.

Tetanus in Newborn Infant: Favorable Results of Serum Treatment. G. Giomo.—p. 440.

Thoracentesis and Pneumothoracocentesis in Common Practice. B. Boggiani.—p. 446.

**Pain After Appendectomy.**—Pieri states that in the course of the last five years thirty-six patients have complained to him of persistent pain in the right iliac fossa after an appendectomy for either chronic or acute appendicitis. In the majority of the cases the pain began several hours after meals. The

roentgen study of the cecal region failed to show any pathologic changes of the cecum. A right vertical laparotomy showed that in four cases pain was caused by the presence of post-operative adhesions, removal of which induced recovery of the patients. In thirty-two cases one of various pathologic conditions (chronic colitis, simple, tuberculous or acute typhilitis or ileotyphlitis, mobile or atonic cecum and cecal neuralgia) existed. Resection of a segment of 2 or 3 cc. of the ileocolic plexus between two ligatures and through a right vertical laparotomy induced recovery of the patients, which was verified by a follow-up observation. In Italy the operation is known by the author's name, since he is the originator. Permanent satisfactory results have been reported from several Italian hospitals.

### **Radiologia Medica, Milan**

25: 779-880 (Sept.) 1938. Partial Index

Roentgenologic Aspects of Round Images of Pulmonary Field. L. Galavresi.—p. 779.

\*Acquired Posterior Sinistocardia and Special Deformation of Trachea: Further Study. G. Giordano.—p. 820.

Roentgenography of Larynx in Anteroposterior Position: Technic and Results. L. Ciurlo and A. Oliveri.—p. 834.

Roentgenologic Aspect of Early and Advanced Gas Gangrene. A. Grilli.—p. 843.

#### **Acquired Posterior Sinistocardia.**

Giordano describes a rare form of tuberculous fibrothorax with permanent lateral posterior displacement of the mediastinum and mediastinal organs, especially the heart and large blood vessels. In the roentgenograms of the thorax which are taken in the latero-lateral position, the cardiovascular shadow shows at the paravertebral region separated from the sternal wall by lung tissue. The author reports four new cases. All the patients were adults suffering from pulmonary tuberculosis with fibrothorax, which developed spontaneously or after artificial pneumothorax or a surgical operation in pleural empyema. Stabilization of fibrothorax and subsequent transposition of the heart to the left had taken place in all cases during either youth or childhood. All had acute bronchiectasia. Bronchography showed that the lower and middle lobes of the lung were emphysematous and displaced to the left, between the sternal wall anteriorly and the cardiovascular shadow posteriorly. The esophagus, especially the thoracic segment, was dilated and retracted to the back in two cases and to the left in two cases. There was no stricture of the esophagus. The trachea, its bifurcation and the left bronchi were displaced to the left and greatly dilated and deformed in two cases, in one of them to a large extent. The author advises further study of the subject in order to determine the mechanism of production of the special displacement of the mediastinum and mediastinal organs in this form of tuberculous fibrothorax.

### **Klinische Wochenschrift, Berlin**

17: 1353-1384 (Sept. 24) 1938. Partial Index

Comparative Investigations on Methods for Determination of Capillary Resistance. T. Jersild and A. Elmby.—p. 1359.

Question of Benign Lymphocytic Meningitis. H. Glatzel.—p. 1360.

Coli-Infection (Colibacillosis of Duodenum). W. Grunke.—p. 1362.

\*Physiology and Pathology of Intermediary Fat Metabolism: Influence of Succinic Acid on Diabetic Ketosis. F. Müller and H. Buchwald.—p. 1364.

Experimental Production of Lipomatosis. K. Kuré, T. Sahara and S. Okinaka.—p. 1366.

Value of Pallida Reaction According to Gaechtens for Serologic Examination of Cerebrospinal Fluid for Syphilis. T. M. Vogelsang.—p. 1370.

#### **Influence of Succinic Acid on Diabetic Ketosis.**

Müller and Buchwald state that the literature contains contradictory reports about the effect of succinic acid on diabetic ketosis and so they decided to investigate this problem on a considerable number of their patients. In doing this they not only determined the elimination of ketone bodies in the urine but also examined the ketone content of the blood several times each day. Summarizing their observations, they state that the clinical examination of the succinic acid therapy of diabetic ketosis, which was recommended by Koranyi and Szent-Györgyi, revealed that the oral administration of succinic acid, even if continued for weeks, does not compensate a diabetic acetonuria. They did not even observe a temporary reduction in the daily ketonemic curve.

Moreover, the typical ketonemic curve observed in diabetic patients, after they have been subjected to a fat tolerance test, could not be influenced in the antiketogenic direction by the administration of succinic acid.

### Münchener medizinische Wochenschrift, Munich

85: 1465-1496 (Sept. 23) 1938. Partial Index

Permanent Results After Transurethral Electrosurgical Resection of Prostate. B. Reiser.—p. 1467.

\*Relations Between Varicella and Herpes Zoster. V. Hourand.—p. 1468. Poisoning Caused by Extract of Arnica in Alcohol. O. Merdinger.—p. 1469.

Method and Aim of Psychotherapy. M. H. Göring.—p. 1472.

Impairment of Procreative Capacity Following Injection Therapy of Hernia. R. Goldhahn.—p. 1475.

**Relations Between Varicella and Herpes Zoster.**—Hourand reports the clinical history of a woman aged 50. He regards this case as important in connection with the problem of the relation between varicella and herpes zoster. The woman developed herpes zoster with the typical symptoms: strictly localized vesicles of various sizes, reddishness and swelling of the skin with great painfulness; the left eye was involved. This attack of herpes zoster was followed a few days later by varicella. The author reviews the literature on the relation between varicella and herpes zoster, citing the concurrence of these two disorders in the same cases but also the development of varicella in persons who had come in contact with persons having herpes zoster and vice versa. After mentioning serologic and immunologic investigations on the etiologic relation between the two disorders, he says that several authors reject the identity of the viruses of varicella and herpes zoster. Some cite the successive appearance of varicella and herpes zoster after intervals of several months as evidence against such an identity but others believe that in such cases the causal agent of varicella, as a dermatotropic virus, confers immunity only on the skin, whereas the neurotropic virus of herpes zoster confers immunity only on the nerves. However, this partial immunization is regarded as the exception and the general immunization as the rule. Returning to the reported case, in which herpes zoster and varicella concurred, the author says that dermatologists have referred to these cases as herpes zoster generalisatus. However, he agrees with von Bokay, Netter, Haslung and others, who reject this term, because in his patient the vesicles were not arranged along the course of certain nerves.

### Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

82: 4295-4410 (Sept. 3) 1938. Partial Index

Myxedema of Heart. E. Behr and J. Mulder.—p. 4303.

Changes in Sensitivity of Uterus Toward Posterior Pituitary and Ergot Preparations Under Influence of Sex Hormones. J. H. Reisel.—p. 4310.

\*Care for Soft Parts During Delivery by Practitioner. J. Baart de la Faille.—p. 4315.

**Care for Soft Parts During Delivery.**—Baart de la Faille assumes an antagonism between the uterus and the soft parts during delivery. The violent pain of the period of dilatation is only partly the result of the uterine contractions. Anxiety and cold cause an extremely painful spasm and this inhibits the labor pains and the dilatation of the os, real rigidity of the os being extremely rare. By adequate heating of the bed and the room, much pain can be saved; the same applies to the use of antispasmodics and analgesics. The author found that with the increasing variety of these drugs the uterine action can be utilized to full advantage, weakness of uterine contractions occurring far less and solution of posterior pituitary being only rarely required. The first stage of labor, the period of dilatation, can be shortened in a considerable percentage. The uterine contractions during expulsion, although less painful, likewise are acted on favorably by these medications, the difficulties of expulsion becoming far less if nature is left to have its own way. The process of distending the soft part thus becomes much more gradual and the indication for extraction by forceps becomes much less frequent. Among the results of excessive distention the author differentiates prolapse from rupture, the former ensuing after forcible distention of the pelvic diaphragm, the latter being limited to the perineum. Slow distention of the pelvic diaphragm pre-

vents a prolapse and slow dilation of the vulval ring reduces the danger of a rupture and the necessity of a suture. The author is skeptical of the value of suturing the perineum. However, he emphasizes that lifting of heavy objects should be avoided for six weeks after delivery.

### Hospitalstidende, Copenhagen

81: 861-888 (Sept. 6) 1938

Acute Porphyria Originated During Hospitalization: Case. A. Eldahl.—p. 861.

Porphyries and Clinically Applicable Methods for Their Establishment. A. Eldahl.—p. 864.

\*Symptomatology of Acute Porphyria and Classification of Porphyrias. A. Eldahl.—p. 871.

Essential Fibrogenic Hemorrhagic Diathesis. N. I. Nissen.—p. 879.

**Acute Porphyria and Porphyrias.**—Eldahl says that acute porphyria is a well defined disorder of acute onset, the main symptoms of which may be violent abdominal pain, constipation (in rare cases diarrhea), organic disorder of the cerebrum and medulla (insomnia, psychosis, multiple pareses), hepatic and renal insufficiency and elimination of porphyrin and chromogen in the urine. The symptoms of disorder of the cerebrum and medulla especially mark the disease and resemble those in encephalitis and poliomyelitis. Acute porphyria is ascribed to a congenital and hereditary anomaly in the intermediary metabolism, a latent or relative insufficiency of the porphyrin synthesis, which can often become absolute. The synthesis probably takes place in the liver. The immediate cause may be infections, often mild infections, overexertion, psychic attack or chemical substances in small amounts. The prognosis is unfavorable; the mortality is about 70 per cent. About 70 per cent of the patients are women, mostly between the ages of 20 and 30; no case under the age of 15 has been reported. Patients with porphyria are often dark skinned but without hypersensitivity to light. Anatomopathologic examinations show slight cirrhotic changes in the liver, in some cases hemosiderin deposits, acute nephritic changes in the tubuli contorti of the kidneys and interstitial leukocyte accumulations, signs of obliterating phlebitis in the kidneys and other organs, and in some cases slight hemorrhages in the cerebrum. In many cases diet treatment has been given such as was formerly generally applied in hepatic and renal disturbances; in the author's personal case of acute porphyria, which originated during hospitalization, insulin and dextrose was administered. Porphyrias are classified in two groups: (1) without symptoms, (a) familial hereditary, constant or periodic, (b) symptomatic, in fever, anemia and so on, (c) medicamentous, after arsenamine and sleeping powders; (2) with symptoms, (a) in porphyria, (b) toxic, after arsenic, lead, sleeping powders and so on, (c) in hydroa vacciniforme.

### Ugeskrift for Læger, Copenhagen

100: 989-1014 (Sept. 1) 1938

\*Are Primary Epidemic Alveolopneumonia and Psittacosis Same Disease? R. K. Rasmussen.—p. 989.

Paroxysmal Myoplegia: Case. J. E. Poulsen.—p. 998.

Plummer-Vinson's Syndrome: Case. H. Videbech.—p. 1001.

**Epidemic Alveolopneumonia and Psittacosis.**—Rasmussen concludes from the account of the sixty-eight cases of primary epidemic alveolopneumonia observed in the Faroe Islands in September, 1933 (Arthur A. Rasmussen, *Ugeskrift for læger*, 1934) that the disease is clinically like psittacosis and has much in common with it epidemiologically. The two diseases affect the same age group and cause about the same mortality. However, while psittacosis is a disease of fall and winter, primary epidemic alveolopneumonia occurs almost exclusively in the month of September and affects six times as many women as men, and particularly pregnant women. The incubation period is unknown. The agreement between the time of the catch of the young procellarians (storm birds) and of the incidence of primary epidemic alveolopneumonia suggests that the source of infection may be in these birds, in which case the infection must be transmitted in the plucking and cleaning of the birds. The author also calls attention to the resemblance of this disease to other disorders, such as streptococcal pneumonia and streptococcal sepsis, and in its milder form to the initial fever of tuberculosis.

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## SPONDYLOLISTHESIS AS AN ETIOLOGIC FACTOR IN BACKACHE

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Spondylolisthesis may be defined as subluxation of a vertebra, usually forward, and most commonly in the lumbosacral region, where it may produce narrowing of the pelvis. Backache is its most common symptom and forward and downward displacement of the lumbar spine its most common deformity. Recognized in 1853 by Killian as a clinical entity, spondylolisthesis was considered a rare condition and one that most commonly affected women. I am convinced that this deformity has escaped the attention of the general profession and that it will become an increasing factor in solving the problem of the relief of chronic backache.

In my experience males are afflicted in the majority of cases, which is contrary to the earlier teachings. I believe that trauma and congenital defects are the important etiologic factors in spondylolisthesis and that obesity, occupational strain and pregnancy may aggravate or produce the symptoms and increase the deformity. Old injuries, sustained months or years previously, may be the (unrecognized) factors which have produced the subluxation, but the most important factors are congenital anomalies which result in weakness in the lumbosacral region.

General practitioners are often called on to fix responsibility for, and to estimate the duration and degree of, such disability. On relief of symptoms they are in a position to return the patient to his occupation and to adjust a fair rate of compensation. In venturing an opinion in cases in which compensation is sought for disability due to chronic backache following overlifting or back injuries, and in cases in which malingering must be considered, I would remind them of the following statement I made before the American Orthopaedic Association in 1931: Pain in the lower part of the back, which is relieved by rest, aggravated by work and associated with industrial injury, suggests the possibility of "railroad spine," traumatic neurosis, and so on, yet these disorders are commonly complained of by patients with spondylolisthesis whose appearance is often apparently normal and who seem to be enjoying undeserved benefits. While in my experience in the neighborhood of only 7 per cent of such cases have been diagnosed previously, present knowledge of the deformity makes it possible for the physician to recognize it,

ascribe responsibility to the factors involved in its production and relieve the symptoms to a larger extent.

Time and space cannot be given in this paper to a complete review of the literature. Killian, as has been said, first recognized the deformity and believed that it resulted from caries and inflammation. In 1866 Blake reported the first case in the United States, that of a multipara who had gained 100 pounds (45 Kg.). Neugebauer in 1844 studied museum specimens and, although he recognized congenital defects, believed trauma to be the principal etiologic factor. In 1897 Lovett described the first case of traumatic spondylolisthesis; his and Gibney's patient (both males) were included in the first six males in a series of 125 patients whose cases had been recorded in the literature up to 1900. Asbury reported on spondylolisthesis in 1927 and felt that it was a definite factor in the production of backache.

The apparent rarity of spondylolisthesis is due to failure on the part of the average examining physician to recognize the deformity. In 1920, for example, only one diagnosis was made of spondylolisthesis at the Mayo Clinic. The number of diagnoses of spondylolisthesis has increased *pari passu* with the increase in our clinical and roentgenologic skill and experience. In 1937 alone eighty-one cases were recognized at the clinic. During the preparation of this paper I saw three patients with spondylolisthesis in a single day.

The subluxation is frequently recognized from inspection of the back alone (fig. 1); the location and grade of the deformity and the type of congenital defect present are determined from examination of lateral and anteroposterior roentgenograms.

I have reviewed a series of 583 cases of spondylolisthesis seen at the clinic and am presenting an exhibit, consisting of roentgenograms and models, at this meeting, which demonstrates the location and grades of the deformity and various methods of treatment. Any physician who visits this demonstration may in a few moments familiarize himself with the clinical and roentgenologic appearances and have at his command the means of relief of symptoms. There is but little justification for continued lack of recognition of this deforming and disabling lesion.

### CHIEF COMPLAINTS

Backache was the chief complaint in more than 80 per cent of 583 cases. Pain was projected to the sacroiliac area, hips and legs in 17 per cent of cases; an additional 7.7 per cent of patients had pain in the legs only, and less than 2 per cent complained of deformity, stiffness or paralysis. Although some of the patients may have had tingling and numbness, weakness or a feeling of stiffness in the legs, true paralysis was rarely found. The average duration of symptoms was 7.5

From the Section on Orthopedic Surgery, the Mayo Clinic.  
Read before the Section on Orthopedic Surgery at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

years; the shortest duration was one day, the longest fifty years. Although it is difficult to understand, 10 per cent of the patients had no complaint and the recognition of the lesion was incidental to examinations for other diseases or deformities. The typical complaint was of backache, with disability on hard labor or on

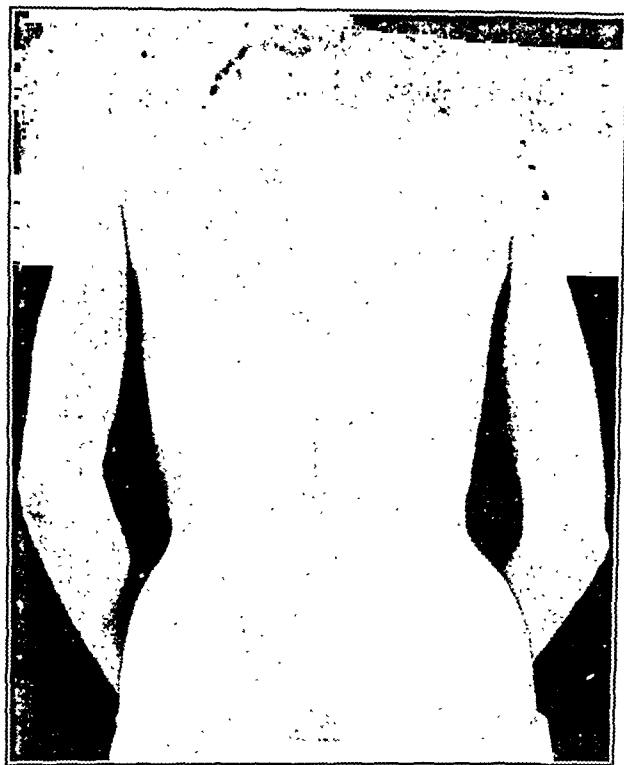


Fig. 1.—Typical deformity of spondylolisthesis, showing depression, and forward and downward displacement of lumbar spine.

stooping and lifting. Slight stiffness and weakness of the back or pain in the legs with relief of symptoms by rest, especially recumbency, was a marked feature (table 1).

#### DIAGNOSIS

In many cases it is possible to make the diagnosis following inspection and palpation. A prominent spinous process and sacrum with lordosis due to forward and downward displacement of the spine and slight muscle spasm are often sufficient evidence to make one suspicious of spondylolisthesis. With lesser degrees of deformity these signs may be unrecognized, but they are always present in grosser displacements, when the shortened torso, prominent erector spinae muscles, broad-appearing pelvis, and abdominal crease accentuate them. Patients with extreme types of spondylolisthesis may list to the side or may waddle when they walk, and the ribs may rest on or telescope into the pelvis; in such cases the diagnosis may be made from inspection alone. Proctoscopic examination may reveal a narrowed pelvis as a result of a hard, fixed mass projecting forward from the spine; in women this may cause difficult labor at childbirth. Pain on lifting and stooping, on being jarred and on carrying heavy objects, which pain is relieved by recumbency, is the common subjective symptom. A few patients have noticed a decrease in height.

Although I feel confident that the diagnosis can be made from these observations, as has been said one must rely on the roentgenologic examination for accurate grading of the degree of deformity and for deter-

mining the site affected and the type of anomalies present, which may be factors in its production. Roentgenologic examination will exclude tuberculosis, fractures, arthritis and tumors. Anteroposterior roentgenograms cannot be relied on to disclose forward displacement; lateral roentgenograms permit gaging of the exact degree of deformity.

Roentgenograms should include the lumbar spine and sacrum. Those familiar with the interpretation of anteroposterior roentgenograms may note the shortened lumbar spine, the superimposed fifth lumbar vertebra on the sacrum, the cocked-up spinous processes, separation of the neural arch, and spina bifida. In the lateral roentgenograms the degree of subluxation may be determined and graded 1, 2, 3 or 4, as in figure 2. To differentiate traumatic from congenital deformities may require roentgenograms taken at an angle of 45 degrees. Smooth, jointlike fissures are usually congenital, whereas irregular, sharp outlines are more suggestive of fracture. One also notes the angle and width of the lumbosacral joint, the condition of the promontory of the sacrum (whether rounded or elongated) and the presence of lipping along the margins of the vertebral bodies. Sclerosing of the articular facets, the length of the neural arch, evidence of fracture or of congenital deformity such as separation, are all observations which influence one's decision as to the etiologic and complicating factors present. A study of the roentgenograms can be carried out best in a moderate degree of light, and special attention should be paid to the contour of the spinal canal where the displacements are often more readily made out. The fifth lumbar vertebra is commonly found to be wedge shaped and the sacral portion elongated, concave and riding forward on the sacrum. The promontory of the latter may impinge

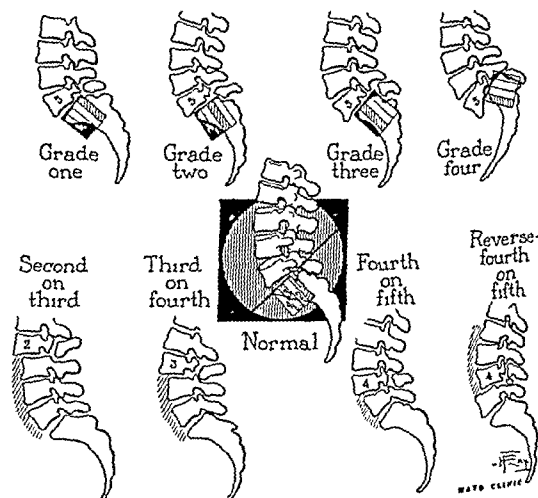


Fig. 2.—Four grades of spondylolisthesis.

between the body and the posteriorly displaced spinous process. The remarkable variation in the lumbosacral angle, which can vary fully 60 degrees, is shown in figure 3.

#### OCCUPATION

About 70 per cent of this series of patients with spondylolisthesis were farmers, laborers or housewives. To my mind this confirms the important effect strain and trauma have on many people, who, had their employment been less strenuous, might have gone through life without symptoms. With the more common use of the roentgenogram an increasing number of

congenital defects have been observed in the region of the fifth lumbar vertebra. When repeated strain or sudden trauma weakens the stability of these parts, symptoms arise and disability results. At the clinic we have observed that more than 10 per cent of patients have spondylolisthesis without being aware of it. The

TABLE 1.—Chief Complaint of Patients with Spondylolisthesis and Duration

Chief Complaint	Cases	Per Cent
Backache.....	368	63.1
Backache and pain in legs.....	99	17.0
Pain in hips and legs.....	45	7.7
Deformity, stiffness, or paralysis.....	11	1.9
Incidental observations.....	60	10.3
Total.....	583	100
Average duration of complaint		
Males.....	7.5 years	
Females.....	7.4 years	
Shortest..... 1 day	Longest..... 50 years	

TABLE 2.—Occupation of Patients with Spondylolisthesis

	Fe- Males	males	Total	Per Cent
Housewives.....	...	157	157	26.9
Laborers.....	126	...	126	21.6
Farmers.....	120	...	120	20.6
Business.....	99	12	111	19.1
Professional.....	31	7	38	6.5
Students.....	24	7	31	5.3
Total.....	400	183	583	
Per cent.....	68.9	31.4		100

inferior articular facets of the fifth lumbar vertebra resting on the superior articular facet of the sacrum, with intact lamina and ligamentous support, should prevent the body of the vertebra from slipping forward. Separation of the neural arch, however, is a very common observation and it is this loss of the support to the facets which seriously impairs the strength of the lumbosacral joint, resulting in subluxation, with strain on the ligaments, stretching or pressure on nerves, abnormal posture, muscle spasm and fatigue. It is interesting to note that not only 70 per cent of our patients who had spondylolisthesis were those that did hard work but almost 70 per cent of our patients were males. Thus the past teaching that the lesion is more frequently found in females is contradicted and the strain of the laborer has supplanted the labor of pregnancy as an etiologic factor (table 2).

AGE AND SEX INCIDENCE

Fifty per cent of our patients with spondylolisthesis were between the ages of 30 and 40 years and 70 per cent were males. The average age of the males was 40.3 and that of the females 43.5 years. The oldest patient was 80 years old, the youngest eleven years (table 3). No doubt the age and sex incidence will vary with the type of practice. I have had roentgenograms of this condition in younger patients sent to me, and Kleinberg has reported one case in a child only 18 months of age.

GRADE OF DEFORMITY AND TRAUMA

A history of trauma was obtained in about 48 per cent of the cases in this series (table 4). The fact that a patient may state that he has had an injury to his back is not sufficient evidence to conclude that subluxa-

tion is the result of the injury. On careful inquiry we have found that the patient sometimes has had chronic backache for months or years prior to the injury but that, following trauma, it had become more troublesome. The type of injury likewise was often of such a nature that it could not possibly have been a factor in the causation of the deformity. In cases in which compensation is of prime importance, the patient may attribute his symptoms to trauma and deny having had backache or disability previously in the hope of obtaining financial gain. In some cases the history furnishes irrefutable proof of the traumatic nature of the condition. When doubt exists as to the cause of pain in the extremities, neurologic examination, including studies with iodized oil and examination of the spinal fluid, may be indicated to rule out the possibility of a cord tumor, slipped intervertebral disk or thickened ligamentum flavum. I attempted to ascertain the effect of trauma on the grade of deformity but was unable to establish a definite relationship. Spondylolisthesis of grade 4 following trauma is no indication that the injury is responsible for the marked deformity, for an equal number of patients with spondylolisthesis of grade 4 had no previous history of trauma (table 4). I have attempted to group the various degrees of subluxation in this series of cases into four grades. The grade or degree of deformity in spondylolisthesis is determined by the examination of lateral roentgenograms; if the fifth lumbar vertebra has slipped forward

TABLE 3.—Age and Sex

Years	Total			
	Males	Fe- males	No.	Per Cent
10-19.....	28	7	75	6.0
20-29.....	66	23	89	15.3
30-39.....	100	46	146	25.0
40-49.....	105	40	145	24.9
50-59.....	70	42	112	19.2
60-69.....	22	20	42	7.2
70-79.....	9	4	13	2.2
80-89.....	0	1	1	0.2
Total.....	400	183	583	100
Average age of male patients.....	40.3 years			
Average age of female patients.....	43.5 years			
Oldest patient .....	80.0 years			
Youngest patient .....	11.0 years			

TABLE 4.—Grade of Deformity in Relation to History of Trauma

Grade of Deformities	Trauma		
	Total Cases	Cases	Per Cent
1.....	237	117	45.5
2.....	138	63	49.3
3.....	29	16	55.2
4.....	18	9	50.0
Not graded.....	141	68	48.2
Total.....	583	278	47.7

less than a fourth of the distance across the lumbosacral joint the spondylolisthesis is graded 1; if it has slipped less than half the distance it is graded 2, if it has slipped less than three fourths of the distance it is graded 3, and if it has slipped more than three fourths of the distance it is graded 4.

Of 442 patients whose degree of deformity was graded, 200, or 45.2 per cent, had spondylolisthesis of



grade 1, and it occurred at the lumbosacral articulation; in forty-seven cases, or 10.6 per cent, the degree of deformity was graded 3 and 4. In 93.4 per cent of the 583 cases in the series the deformity occurred at the level of the fourth and fifth lumbar vertebrae or at the level of the fifth lumbar vertebra and sacrum (table 5).

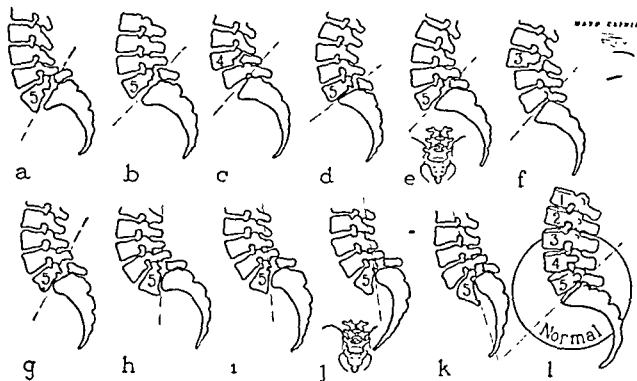


Fig. 3.—Variations in lumbosacral articulation (made from roentgenographic tracings): the lumbosacral angle can vary fully 60 degrees. The sacral angle may be rounded and the inferior aspect of the fifth lumbar vertebra may be concave. Congenital defects of the lumbar region, such as spina bifida and defects of the neural arch, are common.

#### LOCATION OF DEFORMITY

In 82 per cent of the cases in this series the deformity consisted of forward slipping of the fifth lumbar vertebra on the sacrum (table 6). Spondylolisthesis occurs at other levels and in this series it was found that sixty-six patients, or 11.3 per cent, had slipping forward of the fourth lumbar vertebra on the fifth. Less than 1 per cent had involvement of the third and fourth lumbar vertebrae or of the second and third lumbar vertebrae, or of the fifth and sixth lumbar vertebrae, or of the sixth lumbar vertebra and sacrum. One had double displacement, which consisted of two spondylolistheses occurring in the lumbar spine; that is, spondylolisthesis of the fourth lumbar vertebra on the fifth and of the fifth lumbar vertebra on the sacrum. A larger number of the group, twenty-six patients, or 4.4 per cent, had deformity consisting of reverse spondylolisthesis; in this group the vertebra involved is displaced backward instead of forward. This type of spondylo-

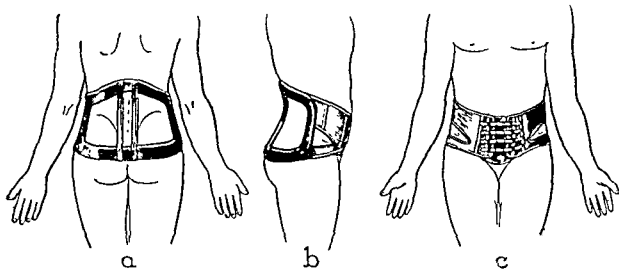


Fig. 4.—Rocking-chair type of back support made of steel and leather.

listhesis gave rise to the definition, which I have stated previously, "spondylolisthesis is a subluxation, usually forward, and most commonly in the lumbosacral region, where it may produce narrowing of the pelvis."

#### TREATMENT

In those cases in which spondylolisthesis occurs as a result of trauma and this is recognized immediately, an attempt should be made to reduce the deformity

by traction and prevent its recurrence by casts. In cases in which the patient is placed in a recumbent position and traction, by means of Buck's extension, is applied, some improvement in the position of the vertebral bodies and relief of symptoms may be expected. With the legs elevated and at right angles to the thighs, and with the thighs at right angles to the recumbent spine, the weight of the torso may be utilized in pulling the vertebral bodies into better position. The insertion of a Kirschner wire through the lower end of the femur maintains this position easily and the danger of irritation of skin is obviated. This position is maintained for six weeks, and following this a plaster cast may be applied, with the legs in extension, in the form of a double spica cast extending up to the axilla. This permits the patient to be moved about or turned over on his abdomen or side; by so doing the occurrence of pressure sores is avoided. The patient is kept in this cast for a further period of six weeks. At the end of this time a lumbosacral support is applied and the patient is allowed up and permitted to walk with crutches. Should

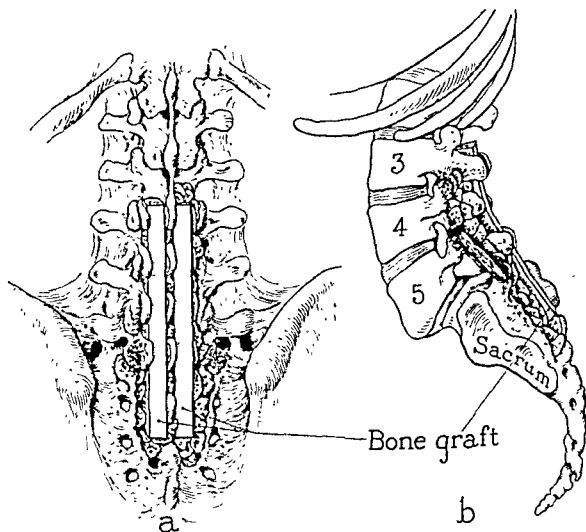


Fig. 5.—Operative procedure to produce strong fusion of the lumbar spine (including third, fourth and fifth lumbar vertebrae and sacrum) by means of double massive bone grafts, multiple bone chips and cancellous bone.

there be recurrence of the subluxation, the spine is better fused by bone grafting, as will be described in a subsequent paragraph.

As some patients do not have symptoms or have only mild symptoms that do not cause disability, a corset reinforced by stays to support the lumbosacral spine is all that is required. In the treatment of women, we employ a strong reinforced corset and, for men, a rocking-chair or canvas belt reinforced with steel type of support (fig. 4). Many patients obtain marked relief from such apparatus and continue to carry on their work; in some cases, however, symptoms continue and fusion of the lower lumbar spine and sacrum is then indicated. Most patients who follow a laborious occupation are subject to such repeated strains and injuries that a change of occupation or an operation is necessary. But I wish again to state that there are some patients who in spite of marked deformity, of grade 3 or 4, go on working at hard labor without symptoms. In some of these cases roentgenographic studies may show that the sacrum has built up a shelf to aid in the support of the fifth lumbar vertebra; in

others, arthritic changes have apparently produced fusion in the affected region. It is apparently true that many patients have never known what a normal back feels like and have continued to work in spite of discomfort and pain.

In order to support adequately the lumbosacral subluxation and prevent further displacement, the fusion resulting from operation must be strong enough to stand the stress and strain of hard labor. As the fifth lumbar spinous process is loose and its fusion alone to the sacrum is of no value, one must go above and fuse the third, fourth and fifth lumbar vertebrae and the sacrum securely (fig. 5). To accomplish this an incision is made from the third lumbar spinous process to the second sacral segment and, with a sharp chisel, fragments of bone are turned from the sides of the processes and the laminae. With retractors in place, the chips of bone and muscles are pulled to one side and the laminae scraped so as to carry some of the bone fragments laterally. Packs of gauze soaked in hot saline solution are then placed in the cavities on either side of the spinous processes and attention is given to further roughening of the laminae and exposing the articular facets; the last named, whenever possible, are curetted to remove cartilage from their articular surfaces. As each facet is destroyed, a pack is firmly pressed into

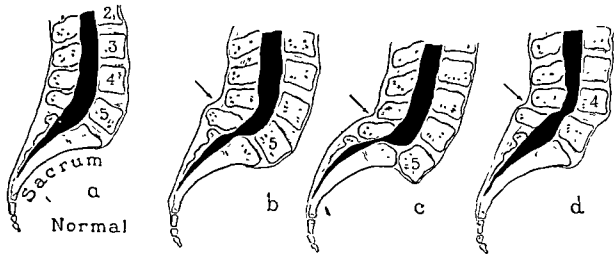


Fig. 6.—Sagittal sections through the lumbosacral area with shading of the dural sac to show pressure on the cauda equina by the displaced vertebra: a, normal spinal canal; b, grade 2 spondylolisthesis of fifth lumbar vertebra on sacrum; c, grade 3 spondylolisthesis of fifth lumbar vertebra on sacrum; d, grade 1 spondylolisthesis of fourth lumbar vertebra on the fifth.

position and the next one is exposed. The object of this roughening is to produce extensive raw surfaces of bone to which the grafts will readily adhere. Care must be taken not to perforate the spinal canal, as spina bifida of the sacrum is often present (fig. 6).

The sacrum is then roughened and a sharp chisel is used to lift thin fragments of bone. When the bed has been thus prepared, it extends from, and includes, the third lumbar vertebra to the third sacral segment. All the soft tissues between the exposed bones are removed. A long incision is made mesial to the tibial crest and a bone graft is removed; this graft, when divided, is of sufficient length to pass from the third lumbar vertebra to the third sacral segment. At times it is necessary to cut grafts with a slight curve so as better to fit them into position; the curved rim of the ilium may be used instead of tibia.

A large curet is employed to remove cancellous bone from the upper end of the tibia; from six to eight masses of cancellous bone are removed and packed in to fill the spaces between the vertebrae. The two grafts are then inserted, one on either side of the spinous processes and over the exposed sacrum, and held by interrupted sutures of number 2 chromic catgut. These sutures approximate the soft tissues, to which numerous small fragments of bone have been left attached, thus

forming a bony bridge over the grafts, denuded spinous processes and laminae. The subcutaneous tissue is sutured with number 1 plain catgut, the needle picking up just enough of the deep fascia to obliterate dead space under the skin. The skin is closed with a continuous dermal suture, and a moist alcohol (70 per cent) gauze dressing of ten or twelve thicknesses is applied.

TABLE 5.—Location and Grade

Location	Grade				Total	
	1	2	3	4	Not Graded Cases	Per Cent
Fifth lumbar on first sacral....	200	117	29	18	114	478 82.1
Fourth lumbar on fifth lumbar	25	19	0	0	22	66 11.3
Third lumbar on fourth lumbar	1	1	0	0	1	3 0.5
Second lumbar on third lumbar	2	0	0	0	0	2 0.3
Fifth lumbar on sixth lumbar	1	1	0	0	0	2 0.3
Sixth lumbar on first sacral....	1	0	0	0	0	1 0.2
Double.....	5	0	0	0	0	5 0.9
Reverse.....	22	0	0	0	4	26 4.4
Total.....	257	138	29	18	141	583
Per cent.....	44.1	23.7	5.0	3.1	24.1	100

A layer of absorbent sterile cotton of sufficient size to extend 4 inches (10 cm.) beyond the gauze is fastened by strips of adhesive tape so as to prevent contamination along the edges.

The patient is then placed on a canvas frame, face downward, and taken to bed; by means of overhead apparatus consisting of ropes and pulleys one nurse is able to raise and lower the patient for various nursing purposes. The patient is kept in the first position, that is on his abdomen, for a period of twenty-four hours and is then turned over several times a day thereafter. Stitches are removed at the end of two weeks. We prefer to keep our patients in bed and on the frame for a period of six weeks, when they are given a lumbosacral support and allowed to walk. When this technic is meticulously carried out, the resulting fusion is excellent, as may be seen from the antero-posterior and lateral roentgenograms, and it extends from the third lumbar vertebra to the third sacral segment. This operation has been performed on ninety-nine patients with gratifying results and we believe that it is the method of choice for all painful and disabling

TABLE 6.—Location

	Cases	Per Cent
Fifth lumbar vertebra on sacrum.....	473	82.1
Fourth lumbar vertebra on fifth lumbar vertebra.....	66	11.3
Third lumbar vertebra on fourth lumbar vertebra.....	3	0.5
Second lumbar vertebra on third lumbar vertebra.....	2	0.3
Fifth lumbar vertebra on sixth lumbar vertebra.....	2	0.3
Sixth lumbar vertebra on first sacral vertebra.....	1	0.2
Double spondylolisthesis, fourth lumbar vertebra on fifth, and fifth on sacrum.....	5	0.9
Reverse spondylolisthesis .....	26	4.4
Total.....	583	100

subluxations of the lumbosacral articulation or other affected spinal levels. There was no operative mortality in this series (table 7).

SUMMARY

In a series of 583 cases of spondylolisthesis involving the lumbar spine the principal complaint was backache or backache and aching in the legs. The average age of the patients was about 40 years and the average duration of symptoms seven and a half years.

About 70 per cent of the patients in this series were males, which contradicts the older teaching that spondylolisthesis occurs most often in females. The condition most frequently affects those who perform hard labor. It may be of traumatic origin or result from congenital abnormalities which have weakened the supporting structure in the lower part of the back.

Although the condition often escapes detection, the deformity can be readily recognized, at times from mere inspection and palpation. It may be proved and graded as to degree of subluxation on examination of lateral roentgenograms. A method of grading spondylolisthesis has been adopted that will permit physicians to transmit the location and extent of subluxation in an easily understood manner.

Congenital and traumatic types of spondylolisthesis must be differentiated, as this is of prime medicolegal significance in dealing with insurance companies and workmen's compensation commissions.

Not all patients who have this deformity complain of symptoms. More than 10 per cent of those included

TABLE 7.—Cases Observed

Year	Surgical	Non-surgical	Total	Per Cent
1918.....	0	2	2	0.3
1920.....	0	1	1	0.2
1921.....	0	2	2	0.3
1922.....	1	5	6	1.1
1923.....	0	6	6	1.1
1924.....	2	3	5	0.8
1925.....	5	10	15	2.6
1926.....	5	10	15	2.6
1927.....	1	15	16	2.7
1928.....	3	16	19	3.3
1929.....	8	24	32	5.5
1930.....	4	33	37	6.3
1931.....	11	46	57	9.8
1932.....	8	33	41	7.0
1933.....	5	39	43	7.4
1934.....	7	65	72	12.3
1935.....	13	42	55	9.4
1936.....	14	58	72	12.3
1937.....	10	71	81	13.9
1938.....	2	4	6	1.1
Total.....	93	484	583	
Per cent.....	17.0	83.0		100

in this series had no symptoms referable to the back. As the degree of subluxation increases to complete dislocation, the shape and angle of the lumbosacral articulation is altered. Paralysis is not commonly found, although paresthesias and referred pain to the saddle area and legs are frequent complaints.

An operation has been devised which prevents further displacement and relieves symptoms, permitting the patient to return to gainful labor.

### ABSTRACT OF DISCUSSION

DR. S. L. HAAS, San Francisco: Dr. Meyerding's paper has so well supplemented his scientific exhibit that there remains little to be discussed. Operations on children may demand special consideration, because a graft over the posterior surface would hinder growth while the bodies would continue to increase in size. There may be an increased force forward, and the displacement may become greater. The anterior bone block across the bodies of the vertebrae would be more satisfactory, as it not only would give the support where it was needed most but would tend to stop the growth of the bodies. I hope that Dr. Meyerding will add something further with regard to the treatment of spondylolisthesis in children.

DR. CHARLES LEROY LOWMAN, Los Angeles: For diagnosis roentgenograms are essential in confirming certain clinical appearances which should tentatively make one suspect the

existence of the condition: (1) the absence of a posterior rounding of the lumbosacral curve on bending forward, (2) an exaggerated lumbar curve on standing, (3) the feeling to the palpating hand when the patient lies prone of a sharp dip forward from the posterior prominence of the first sacral vertebra into a hollow over the lumbosacral junction or (4) inability of the patient when lying supine to hold the extended legs in semiflexion without pain at the region of the lumbosacral junction or a feeling that he is "giving away" at that point. I should like to call attention again to the importance of roentgenograms taken laterally with the patient in the standing position to bring out the slippage in mild grades of this deviation. In severer grades the position of displacement will be fixed by muscle spasm or ligamentous shortening and can be detected readily in the lateral view taken with the patient lying down. However, it should be appreciated that, as the pelvis changes its degree of obliquity from the standing to the lying position and loses usually any lateral tilt which may exist because of short legs or structural discrepancies in the sacrum or ilium, a view showing the actual influence of the gravity load will give valuable information. Dr. Meyerding has called attention to the high incidence of congenital faults in this region; the addition of any unusual stress added to the existing weakness, which may previously have been tolerated, can easily be the factor which produces the further displacement or provokes the pain or disability which brings the patient to the physician. The common existence of flattened interarticular processes on the first sacral vertebra is, I think, an important element, because as increased obliquity occurs in the anteroposterior plane, mechanical locking is decreased and the load on the ilio-lumbar and anterior vertebral ligaments is increased, raising the possibility of displacement under stress. With regard to the operative phase, orthopedic surgeons have all experienced difficulty in obtaining true arthrodesis at this point, and I have been greatly impressed by the value of Dr. Meyerding's procedure in putting in so much bone over a large enough area to obtain this massive repair.

DR. J. ALBERT KEY, St. Louis: I should like to ask Dr. Meyerding to state what patients he operates on and what ones he recommends for conservative treatment.

DR. JOHN DUNLOP, Pasadena, Calif.: I should like to ask what influence the diagnosis has in compensation cases as to the cause.

DR. HENRY W. MEYERDING, Rochester, Minn.: It is interesting to note that backache was the principal symptom in more than 80 per cent of these cases of spondylolisthesis and that in almost an equal percentage of cases the occupation of the patient required heavy labor. The average age of the patients was more than 40 years, and the average duration of symptoms was about seven and one-half years. These studies have proved that the strain of pregnancy is no longer a principal etiologic factor. I believe that congenital anomalies are the principal factors in the production of spondylolisthesis and that the stress and strain sustained by patients whose occupation is concerned with manual labor are exciting factors. The condition occurred in the lumbosacral region in more than 80 per cent of the cases in this series. More than two thirds of the patients were males; this contradicts the previous teaching that the condition occurs more frequently in females. My associates and I have operated in less than a fifth of this series of 583 cases. Ten per cent of the patients had no symptoms referable to the back, and the diagnosis of spondylolisthesis was incidental to examinations carried out for other symptoms. Many of the patients who had not been disabled were relieved of their backache by the use of lumbosacral supports; this type of support is reinforced by steel stays and fits well down onto the sacrum and upward onto the lumbar vertebrae. When the occupation required activity and the patient was likely to have increasing symptoms and deformity with disability, we advised surgical fusion. The operation produces a huge mass of bone, which results in firm, bony fusion of the sacrum and the third, fourth and fifth lumbar vertebrae. Acute traumatic spondylolisthesis is treated by overhead traction by means of a Balkan frame. We have not observed any untoward results in patients who have been treated by the surgical method described. The patients were all adults who had had backache for a number of years.

THE ONE STAGE COMBINED ABDOMINO-  
PERINEAL RESECTION OF THE  
RECTUM

FRED W. RANKIN, M.D.

LEXINGTON, KY.

The choice of offensive against cancer of the rectum and rectosigmoid at the present time indubitably is surgical intervention. That the extirpation of cancer in this location can be done in conformity with the fundamental principles of radical operations for cancer elsewhere is equally true. It is axiomatic, however, that cancers low in the gastrointestinal tract demand an unusually high individualization so far as operative maneuvers are concerned. No one technical procedure is applicable to all malignant growths in this location, and many factors, including coexisting debilitating diseases, the ability of the patient to withstand formidable surgical intervention and the undermining influences of malignant processes in general must influence the choice of operation.

The well known tendency of cancers of the rectum to develop on adenomas and areas of local hyperplasia, the slow evolution of the concurring malignant process, its tendency to be of a relatively low order of cellular activity and consequently to invade lymphatics late, all allow the surgeon a remarkable latitude in the selection of operative plans.

Individualization of treatment is a paramount necessity in dealing with cancer of the rectum, and for this reason no one type of operation is applicable as a matter of routine without an excessive reduction in the operability figures and a probable increase in the mortality rate. To insure that as many as two out of three or even three out of four patients as they present themselves for examination will be subjected to operative removal, one may employ, first, the radical combined abdominoperineal resection or the perineo-abdominal operation in one or two stages; second, colostomy and posterior resection as advocated by Mummery, and, third, local excision with or without segmental resection and with or without preservation of the sphincter.

For the last-named type of operation I have small enthusiasm, believing that a colostomy is a necessary part of any operation which will give a high percentage of satisfactory end results. Colostomy does not entail social ostracism or professional incapacity, but there is a certain stigma attached to it and the preservation of the rectal sphincter in a small group of properly selected cases, namely those in which the cancer is of low pathologic grade and without metastases, is the desire of both surgeon and patient. The great difficulty in making this selection is to tell without resection which growth has remained local and which has metastasized, but the high percentage of glands now found involved in the resected specimens indicates that the crux of the situation from the standpoint of prognosis still remains a question of glandular involvement at the time of operation.

The work of Miles<sup>1</sup> on the lymphatics of the rectum still stands, I think, as a classic on which is predi-

cated the logic for removal of gland-bearing tissues even to the height of the mesentery of the sigmoid flexure. Westheus<sup>2</sup> recently published the report of an exhaustive investigation of the lymphatics of the rectum in relation to the spread of cancer, in which he disagrees with Miles that the downward spread is of frequent occurrence. While this type of spread may permit the utilization of an operation to save the sphincter mechanism in certain closely selected cases, actually the vast majority of invaded lymphatics are in the upward zone of spread, and the most recent investigations by Gabriel, Dukes and Bussey,<sup>3</sup> David and Gilchrist,<sup>4</sup> and others prove conclusively that a higher percentage of invaded lymphatic glands are now being found by more extensive and exhaustive methods of search. In my own series of 139 cases in this study, the glands were involved in 55 per cent of the specimens.

At the St. Mark's Hospital, Gabriel, Dukes and Bussey,<sup>3</sup> making an extensive examination of 100 excised rectums and investigating an average of twenty-eight glands in each case and in some instances as

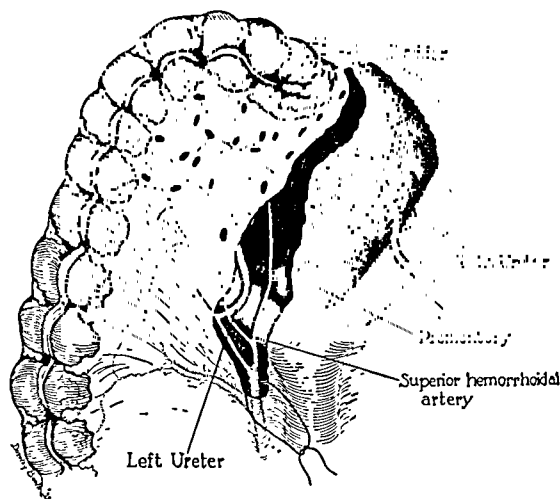


Fig. 1.—Beginning of mobilization and dissection of the pelvis. An incision in the peritoneal covering of the mesentery on its right side has been made from the inferior mesenteric vessels down to the bladder. The right peritoneal leaf is to be dissected further to form one half of the pelvic floor. Ligation of the inferior mesenteric vessel above the superior hemorrhoidal artery is shown. Both ureters are exposed.

many as sixty glands, found that 62 per cent of the resected specimens showed involved glands. David and Gilchrist<sup>4</sup> reported before the American Surgical Association in May 1938 isolation of between fifty and eighty glands to a resected specimen in their series of cases, with evidence of glandular involvement in 70 per cent. These studies seem to indicate accurately that extensive and thorough investigation proves the incidence of glandular involvement to be much higher than was formerly believed, and they emphasize the necessity of extensive removal of gland-bearing tissues.

The principles laid down by Miles<sup>1</sup> for his radical combined abdominoperineal resection, and consummated as radically by Grey-Turner, Gabriel and their British colleagues in their perineo-abdominal resection, more nearly, I think, answer the full requirements of radical surgical intervention than other types of operation.

Read before the Section on Surgery, General and Abdominal, at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.

1. Miles, W. Ernest: *Cancer of the Rectum*. London, Harrison & Sons, Ltd., 1926.

2. Westheus, quoted by Bastianelli, R.: *Deutsche med. Wchnschr.* 63: 1254-1259 (Aug. 13) 1937.

3. Gabriel, W. B.; Dukes, Cuthbert, and Bussey, H. J. R.: *Brit. J. Surg.* 23: 90 (Oct.) 1935.

4. David, V. C., and Gilchrist, R. K.: Personal communication to the author.

The advantages of the combined operation may be summarized as follows:

1. It conforms to the principles of radical extirpation of cancer elsewhere, removing the local growth and tissues in the zones of spread.
2. It permits of variations and modifications to be done in either one or two stages.
3. It may be accomplished either as an abdominoperineal or as a perineo-abdominal operation.

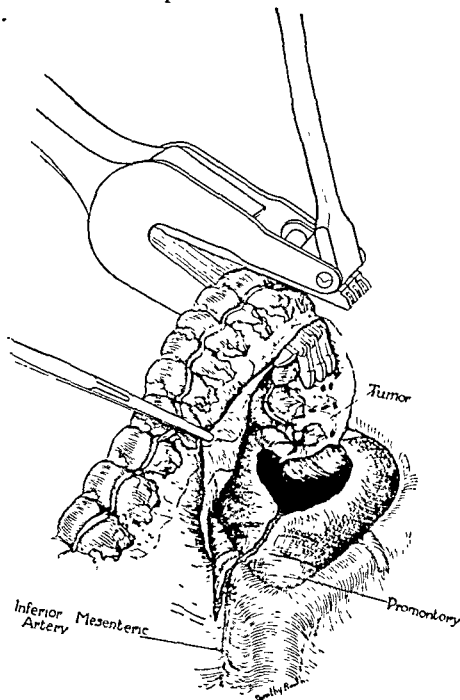


Fig. 2.—The pelvic dissection further advanced. Both the right and the left peritoneal flaps are demonstrated, the tumor is shown at the recto-sigmoid junction, where two thirds of all rectal cancers occur, and the beginning application of the Zachary-Cope de Martel clamp is illustrated. This clamp consists of three independent, biting blades with end catches to hold them in place and is applied in a removable crushing instrument.

4. With increasing experience on the part of the surgeon, the operability curve may be broadened and at the same time the hospital mortality remain below 10 per cent.

5. Five year end results from the clinics of the most experienced advocates of the radical combined procedures indicate a higher percentage of five year cures than for the other types of operation.

6. Only one laparotomy is required, so that time and expense are saved for the patient.

7. The blood supply to the growth may be ligated before the pelvic dissection is undertaken.

8. The procedure is applicable to all ampullary and recto-sigmoidal cancers.

The disadvantages may be summarized as follows:

1. It has been argued that the operation involves a higher mortality than the less radical procedures.
2. The operation bears the stigma of a colostomy.

#### PREOPERATIVE TREATMENT

Meticulous and carefully planned routine pre-operative measures unquestionably greatly facilitate the operative act. The patient should in every instance (except when acute intestinal obstruction is present) be hospitalized from five to seven days. It is my plan not to have the patient in bed but to allow him to be ambulatory and to direct all efforts toward decompression of the bowel by means of purgation and enemas. These measures are continued until twenty-four hours before operation, when the patient is given camphorated tincture of opium or lead and opium pills to allay peristalsis. I do not use continued

purgation but prefer to give one large dose of castor oil at the beginning of the preparatory period and follow this by multiple daily washings with physiologic solution of sodium chloride. The usual tests are repeated as often as necessary to insure proper balance of the blood chemistry. Transfusions are resorted to when they seem necessary but are not used as a matter of routine before operation. A large amount of dextrose in the diet is insisted on. The routine cardiac and renal function observations are made, and rehabilitation during this period of decompression is forwarded by whatever means are possible.

#### TECHNIC

The abdomen is opened through a long low median incision which passes from the symphysis to a point about 2 inches above and to the left of the umbilicus. In all, the incision is about 10 to 12 inches in length. As soon as the peritoneal cavity is open the left hand is thrust upward to the liver to begin exploration of the abdomen from above downward. The surfaces of the liver are felt, the gallbladder is examined and the glands along the aorta, the common iliac vessels and, lastly, the growth itself are explored. The growth is tested for mobility, its operability determined and the procedure of resection begun.

The importance of the deep Trendelenburg position cannot be overemphasized, since it facilitates the packing off of the pelvis, which is exposed by a spreading, self-retaining retractor. In a woman the uterus is held up out of the top of the wound with a blunt hook, so that the bottom of the pelvis is easily exposed.

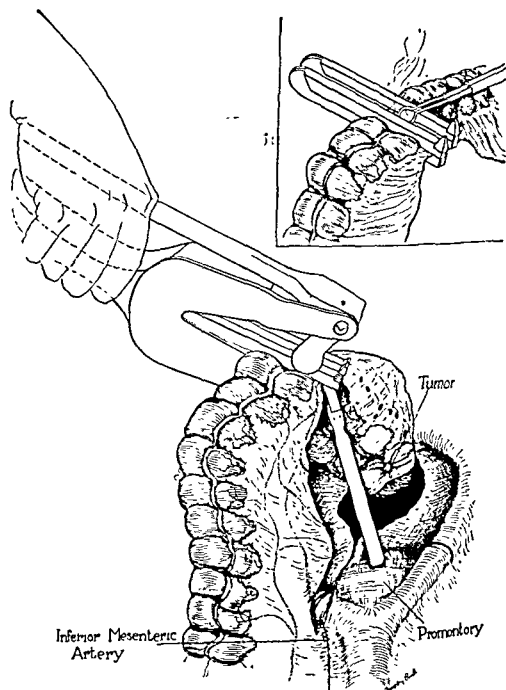


Fig. 3.—The dissection completed, the clamp in place and the end catches closed. The inset shows the middle blade removed and the division of the bowel by the cautery. Adequate blood supply to the proximal end, which forms the colostomy, is demonstrated under visual inspection.

The loop of the sigmoid flexure is drawn to the right to expose the natural adhesions between the peritoneum and the mesentery of the sigmoid flexure. These are divided by sharp dissection. It will be remembered that the colon ascends in fetal life from the pelvis and usually lies in the left side of the pelvis; as it emerges

the lateral part of the parietal peritoneum and the mesenteric covering are fused at the level of the pelvic brim.

After mobilization of the sigmoid flexure, the peritoneal covering of the left side of the mesocolon is divided about  $1\frac{1}{2}$  inches from its peritoneal reflection from a point opposite the main trunk of the inferior mesenteric vessels downward into the pelvis. This

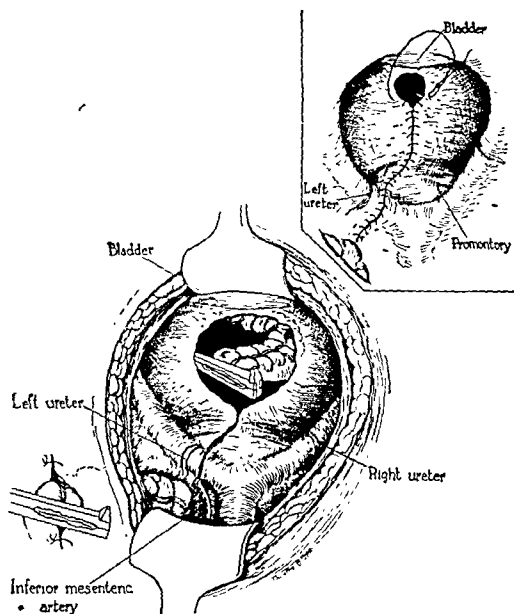


Fig. 4.—The colostomy established through a stab wound in the left groin. The tumor and the distal segment of bowel are dropped down into the pelvis, and a new pelvic floor is made by closing the peritoneal flaps. In the woman the tubes and ovaries give additional support to the pelvic floor. It is essential that all raw surfaces be covered.

incision is then extended laterally below the brim of the true pelvis and well into the parietal peritoneal covering and from there anteriorly to encircle the pouch of Douglas in the female or the rectovesical space in the male. The anterolateral portion of the peritoneum is then dissected free by blunt dissection to form the left half of the new pelvic floor. At this point the left ureter is identified, having been clearly exposed by the removal of the lateral reflection of the parietal peritoneum. It will be noted that a great deal of the mesentery has been denuded of peritoneum by this procedure. All of the mesentery of the lower two thirds of the sigmoid flexure is sacrificed.

The right side of the pelvis is then exposed, and in a similar manner sufficient peritoneum is dissected free to form the right half of the new pelvic floor. The right ureter is then isolated, although there is much less danger of ligation on this side because it normally courses farther outward over the large vessels. The gland-bearing tissues and retroperitoneal fat from the bifurcation of the aorta outward and down over the hollow of the sacrum are swept mesially to insure a clean dissection of the entire pelvic lymphatic supply of the rectosigmoid.

Dissection is then carried forward into the tissue plane which separates the seminal vesicles and prostate or the posterior vaginal wall, as the case may be, from the anterior surface of the rectum. With this mobilization carried well down into the pelvis, an anterior peritoneal flap is then created to complete the new pelvic floor.

With the hand placed in the hollow of the sacrum, finger dissection is carried still farther downward, with

a division of the posterior ligamentous attachments to the point where the fascia propria of the rectum fuses with the periosteum of the sacrum at the sacrococcygeal articulation. Lateral dissection is carried out with the scissors, visualization being aided by the Kameron light. In severing the lateral ligaments one must remember that the middle hemorrhoidal arteries are concealed in them. Usually they are so small that hemorrhage does not occur, but in about 10 per cent of the cases they are found to be medium-sized vessels which require ligation.

The blood supply of the entire segment of the bowel is then identified, caught in clamps, divided and doubly ligated, the inferior mesenteric vessels being tied below the superior hemorrhoidal branch. The field is carefully inspected to avoid inclusion of the left ureter in this clamp. The left colic artery is protected to insure adequate blood supply to the proximal end of the bowel, and under direct vision the point of division of the bowel is located with relation to the pulsation of the small vessels. The vascular arcades are ligated individually, as the mesentery is then divided up to the intestine. The de Martel-Cope clamp is applied to the bowel after demonstration of an adequate blood supply to the proximal end. After the bowel is crushed the two end blades of the clamp are left on, the middle blade removed and the bowel divided with the cautery. The pelvis is cleanly dissected, and the entire loop of bowel to be removed is thrust down into it and covered over by the newly formed pelvic floor. The peritoneal flaps are approximated with a running suture of chromic catgut, and this is reinforced with a second line of sutures. When the patient is a woman the

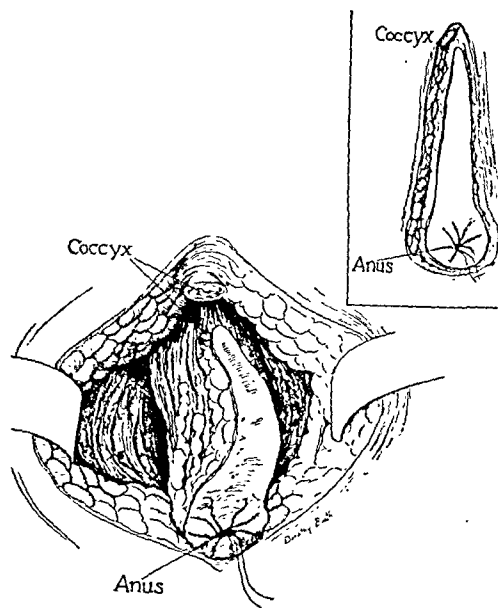


Fig. 5.—The beginning of the posterior removal of the entire bowel segment. The rectum is closed with a purse string suture, and two curved incisions extending from the coccyx to the center of the perineum encircle it. The coccyx is removed, the perirectal fat is included in the dissection and the levator ani muscle is sacrificed.

uterus, tubes and ovaries are dropped over the line of sutures, further strengthening it.

The next step is the colostomy. I prefer to follow Miles's original procedure and make the opening in the left groin through a separate incision, closing the midline incision. A circular piece of skin about  $1\frac{1}{2}$  inches in diameter is excised from the anterior superior



spine of the ilium on a line with the umbilicus. After removal of the skin the incision is carried directly downward through the musculature of the abdominal wall, and just enough opening is made to allow the proximal end of the bowel to be drawn out easily and yet to be held snugly by the peritoneum. Two or three interrupted sutures between the peritoneum and the

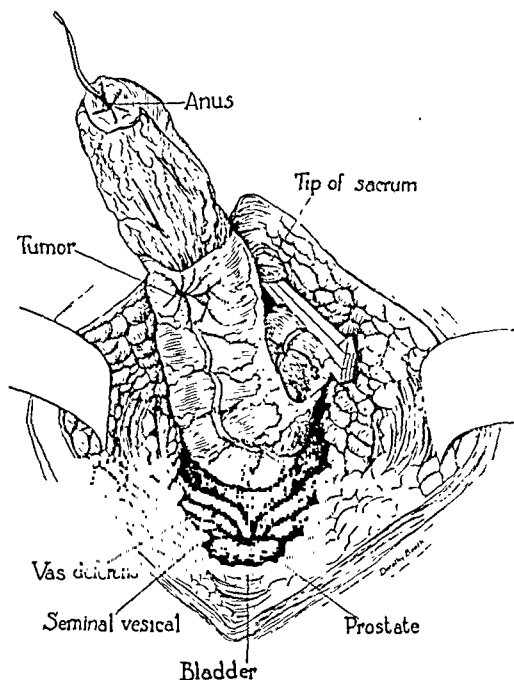


Fig. 6.—The pelvis has been opened by division of the fascia propria, and the bowel segment containing the tumor is being delivered.

epiploic appendages and mesenteric fat of the bowel are all that hold it in the wound. Care is taken not to penetrate the coats of the bowel itself with sutures. The de Martel-Cope clamp blade is left on, obstructing the bowel for thirty-six hours, until adhesions have formed between its peritoneal surface and danger of leakage is past. The wound is closed in layers and the colostomy opening is surrounded by petrolatum gauze packing and incorporated in a separate set of dressings.

The second stage is done with the patient in the posterior resection position with the hips well elevated. The anus is closed with a running suture of strong silk. Two semilunar incisions extending from just above the sacrococcygeal joint to midway of the perineum are made encircling the anus. The dissection on each side includes the fat in the ischioanal fossa. Dissection is carried down laterally on both sides to and through the levator ani muscle before the anal canal is separated from the vagina in the woman or the prostate in man.

The lowermost part of the dissection is done by cutting through the perineal body separating the rectum from the vagina or prostate. Practically all the second stage is finished before the pelvic cavity is again opened. The sacrococcygeal articulation is divided, the coccyx being removed in all cases. The branches of the middle sacral artery frequently bleed at this point and should always be ligated. The fascia propria is then divided to open the cavity of the pelvis. The whole segment of bowel is delivered, the pelvic cavity filled with a sponge saturated with mercury bichloride solution and the bleeding points all carefully and accurately ligated.

The cavity left by the resection is filled with a gauze pack encased in a sheet of oiled silk. This pack serves two purposes, first to support the pelvic floor and, second, to prevent oozing. One half is removed at the end of thirty-six hours and the remainder at the end of seventy-two hours. The silk shield prevents any adhesions to the tissues and makes the removal of the pack painless. The wound is closed very loosely with silkworm sutures. An attempt is made only to cover the open end of the sacrum where the coccyx was disarticulated. The entire wound is expected to heal by granulation.

#### POSTOPERATIVE CARE

All patients are given a transfusion of 500 cc. of citrated blood immediately after operation. Forty-eight hours after the removal of the pack from the posterior part of the wound, irrigations of the cavity with warm saline solution or potassium permanganate solution are started, to be given daily. The colostomy opening is treated in the ordinary way without irrigation, and the bowels usually move spontaneously after the fourth day. Hydration and feeding are usually by venoclysis until seventy-two hours has elapsed. Once gas is passed from the colostomy, food is given by mouth. Healing by granulation is slow but is usually complete in from six to eight weeks except for a small, superficial area.

#### OPERABILITY AND MORTALITY

Since June 1934, when I did the first Miles operation in this series, I have operated on 139 private patients for cancer of the rectum and rectosigmoid. Of the resections, seventy-five were done by Miles's technic

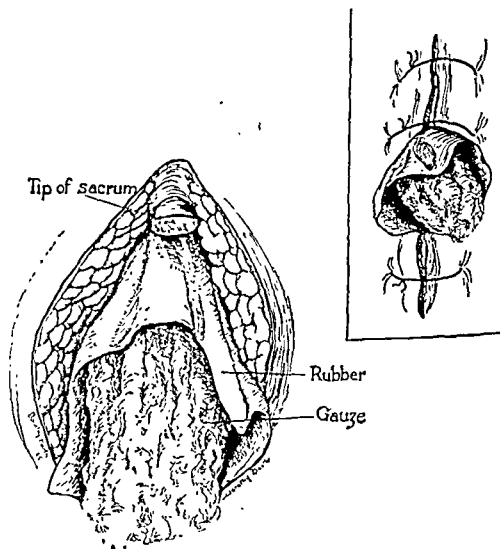


Fig. 7.—The inset shows the wound closed loosely with interrupted sutures, while the main figure shows the drainage in place. A huge dam of oiled silk is pushed into the pelvic cavity and filled with gauze packing, the one half of which is removed at the end of forty-eight hours and the remainder in seventy-two hours. The pack not only prevents oozing but supports the pelvic floor until exudate makes it firm. Its removal is painless.

in one stage, six by my own type of two stage combined perineo-abdominal resection and twenty-five by Mummary's operation of colostomy and posterior resection. The Miles operations were done with five deaths, a mortality of 6.6 per cent. The causes of death were pulmonary embolism (confirmed post mortem) in two cases, peritonitis (confirmed post mortem) in two cases and cerebral thrombosis (hemiplegia twelve hours postoperatively) in one case.

Resection was done in 106 of the 139 cases, a resectability figure of 76.2 per cent. Thus it will be seen that approximately three fourths of the resections in this series were done by the one stage combined abdominoperineal method, indicating its applicability in a high percentage of cases in which meticulous preoperative care, careful operative technic and personal postoperative supervision are combined. It is an operation which calls for team work not only in the operating room but in the wards and because of the necessary cooperative management probably will not become a routine operation except in the hands of surgeons in whose practice a large group of rectal cancers are encountered.

#### PROGNOSIS

The prognosis depends largely on extension of the growth, and whether one estimates this by Broders' type of grading or by Dukes' method, the end results are much the same. Fortunately, the largest percentage of cancers of the rectum are of grades 1 or 2 and remain local a considerable length of time. Statistical data furnish ample evidence that radical extirpation of the rectum by the combined abdominoperineal resection or the combined perineo-abdominal operation gives a higher percentage of five year cures than the less radical procedures. However, one should consider operability percentages along with mortality curves when evaluating postoperative results, for a cautious and not widely experienced surgeon may consider a growth inoperable because of fixation, which a more experienced and daring surgeon would readily attack. It follows that definite attempts should be made to elevate the operability figure by including questionable and borderline cases so long as they do not raise the hospital death rate beyond 10 or 12 per cent.

In October 1935, before the American College of Surgeons, Abel<sup>5</sup> reported on a series of 164 radical operations; 104 of the patients, or 63.4 per cent, were alive and well five years later. Thomas E. Jones<sup>6</sup> of Cleveland presented before the same assembly a series of 151 cases, in 52 per cent of which the patient was living and well five years postoperatively.

The colostomy and posterior resection, a valuable operation applicable in a wide range of cases, has in my hands given a smaller percentage of five year cures. In June 1933, before the Section on Surgery, General and Abdominal, of the American Medical Association, I reported from the Mayo Clinic 300 cases of posterior resection, in 36 per cent of which the patient was well after five years. Mummery reported a higher percentage of satisfactory results from his operation and, using Dukes' grading, found that survivals for all grades numbered 52.5 per cent of the five year cures.

From these figures, if one considers the stage of the tumor at which operation is undertaken, it seems that the curability curve is raised by the radicalness of the operation, and, by the same token, that multiple operations are necessary to insure a high percentage of resections.

Radical surgical intervention may be accomplished more satisfactorily by the combined method of resection, but the utility of other types of operation is undeniable. To both Miles and Mummery the surgi-

cal profession owes a debt of gratitude for their pioneering, fundamental work, and the operations of both men must certainly be included in any surgeon's armamentarium.

#### ABSTRACT OF DISCUSSION

DR. THOMAS M. JOYCE, Portland, Ore.: There is the liability to obstruction when the colostomy is made on the left side, unless the opening between the mesentery of the sigmoid and the parietal peritoneum is closed. I have been unfortunate in having this happen to me twice. Again, in making the opening through the abdominal wall for the colostomy it is very important that the slit through the fascia be adequate, for if this is tight it is likely to cut through into the bowel and there will be an abscess below the skin and in the abdominal wall. I have been unfortunate to have had this experience. I do not use sutures in the bowel. I have seen reports of these abdominal wall abscesses which were thought to be due to diverticula, but I believe they are due to an inadequate opening through the abdominal fascia. I have one more little procedure in the technic of removing the mesentery of the sigmoid which I remove high, in an effort to get all the gland-bearing area, just as thoroughly as I would in removing the axillary glands with a carcinoma of the breast: instead of attempting to put the whole sigmoid retroperitoneally, I remove this segment with the glands, and it usually amounts to about 8 or 10 inches. It is then very easy to put the distal segment retroperitoneally and close the floor of the pelvis without the least difficulty. Next I would mention the care of the colostomy. I do not believe in using any sort of container or rubber bag, such as one so often sees exhibited and advocated. With the usual cleaning out each morning, flushing of the sigmoid, using a pad of cotton over the colostomy opening and a thick canvas square which goes over the colostomy, with elastic bands around the abdomen to hold it in place, one will have no trouble whatever with discharge from the colostomy. Dr. Rankin mentioned that his operability was practically 76 per cent of the patients that come to him. I have a connection with a large municipal hospital at the University of Oregon where we have found the operability to be 23 per cent. At St. Vincent's Hospital, where the private patients come, our operability is 61 per cent. The longest span of life of those who were considered inoperable at the County Hospital was six months. It has been our practice to have adequate preparation of from four to six days, especially in decompressing the bowel, with preoperative blood transfusions, and in the majority of cases in which we are able to have adequate preoperative decompression we are able to do a one stage abdominoperineal resection. However, there are some cases among the elderly in which, even with adequate preparation, we have thought it advisable to do the two stage operation or the Mummery operation in two stages.

DR. HARVEY B. STONE, Baltimore: As Dr. Rankin stated, the Miles type of operation has definite advantages. It is true that it is a formidable procedure but experienced surgeons are performing it with a mortality of 10 per cent. This is not prohibitive considering the grave nature of the disease and the increased prospect of five year cures offered by this operation. One is somewhat surprised to read of the much higher mortality figures reported from some of the German clinics. In no sense of criticism, one may hazard the guess that this difference may be due to another point emphasized by Dr. Rankin, the essential importance of adequate preoperative preparation. Thorough clearing of the bowel beforehand, rest and building up of glycogen reserve, and the free use of transfusion of blood before and at the end of operation are probably more responsible for better immediate results than improved technical maneuvers in the operation itself. Nevertheless, in such a major surgical attack, skill, experience and well organized team work are of the greatest importance, and, as Dr. Rankin has hinted, men whose work does not provide fairly frequent opportunity to acquire these facilities may be reluctant to adopt the Miles operation. The fact that this is a single stage procedure and that it permits early control of the major blood supply of the whole field are other advantages Dr. Rankin has pointed out. But to my mind the greatest argument for the Miles type of

5. Abel, A. Lawrence: Five Year Cures of Cancer of the Rectum by the Radical Abdominoperineal Excision, Surg., Gynec. & Obst. 60: 481-482 (Feb. 15) 1935.

6. Jones, Thomas E.: The One Stage Abdominoperineal Operation for Carcinoma of the Rectum, Ann. Surg. 102: 64 (July) 1935.

attack is that this principle of approach alone allows adequate removal of the zone of lymphatic spread of the disease. Only by this method can one deal with cancer of the rectum in accord with those principles of surgical treatment of malignancy first established for the breast and now regarded as the best that surgery has to offer in the cure of cancer. It is true, as Dr. Rankin and other authorities always point out, that in the field of rectal cancer one cannot restrict oneself to a single method of operating. Variations in anatomic location, size of the lesion and condition of the patient all enter into the decision of the best way to handle each individual case, and certainly the one stage abdominoperineal resection cannot be universally employed. Nevertheless, where it is suitable it remains the best chance of permanent cure, when performed by experienced and competent surgeons. It is not appropriate to talk about details of technic at such a meeting as this, except to compliment Dr. Rankin on his clear and concise description. In only one point do I differ from him, preferring to do the second step of removal of the rectum from below in the exaggerated lithotomy position.

DR. THOMAS E. JONES, Cleveland: At the Detroit meeting eight or ten years ago I read a paper on this subject for this section. It was not very graciously received for the simple reason that it was thought that the procedure was too formidable and the mortality too high. However, it had seemed to me that the fault was not with the operation itself but with the fact that the preoperative treatment in this type of case had been inadequate. Following Miles, I kept these patients in bed eight or ten days and it was apparent that the chronically obstructed bowel could be decompressed with this method just as easily as by colostomy, and I started to do the combined abdominoperineal operation in one stage. It has been very satisfactory in my hands. With regard to the two stage operation, it has been my experience many times that when an exploratory operation was done and the condition seemed inoperable at that time, on reoperation in two or three weeks the condition found would be the same—inoperable. In the last 200 cases I have brought the colostomy out at the midline. The patients seem to like it better. I advise against the use of the colostomy bag but if patients insist on wearing a bag at least they look symmetrical and that is very important for the woman patient. In a series of 300 cases done in one stage, with an operability of 64 per cent, my mortality was 9.2 per cent. I am sure it is not only the technical maneuver, which is after all a small part of this, but also the preoperative care and care of the patient after the operation that contributes greatly to its success.

DR. FRED W. RANKIN, Lexington, Ky.: I am happy to have the gentlemen who discussed this paper agree that colostomy is not such an undesirable companion and is entirely compatible with a useful professional and social life. There are just two or three things to remember about a colostomy. One is that it has to be made properly, and in making it properly one has to take the slack out of the bowel and bring the loop out through as small an opening as is adequate. Secondly, care must be taken to obviate the possibility of herniation either of the mucosa or of the whole bowel. A hernia around a colostomy is very unpleasant. If these two technical steps are taken care of and the patient is put on a proper regimen and has the proper mental attitude toward the colostomy, I can imagine many things that are much more uncomfortable and disagreeable to possess. Dr. Joyce's point about obstruction following the making of a colostomy in the groin is well taken. I have seen this happen occasionally, but I believe the two factors most important in obviating it are, first, to have no raw surfaces in the neighborhood of the dissection which a loop of bowel can slip around and become adherent to; secondly, have a sufficiently large opening for the loop which is being utilized for the colostomy, or to close that lateral gutter with a single, continuous suture during the course of the operation. Also, these cups and general devices which are widely advertised are not only entirely unnecessary but largely undesirable. The colostomy should be adequately attended to and emptied, and the patient is kept on a diet which keeps away from loose stools. I think that proper attention to the colostomy in the morning, or occasionally in the evening, depending on the

patient's own choice, and an ordinary elastic supporter with a pad of cotton or gauze over the protruding mucous membrane are better. I agree with Dr. Stone as to bladder involvement being an indication of inoperability. I have four times removed a large portion of the bladder with a carcinoma of the low sigmoid successfully so far as the operative mortality is concerned, but the longest existence after any of these procedures was two years, and it is hardly worth while, to do a large, difficult job, when a palliative operation to relieve the patient would probably have done just as well. I question whether it is worth while attacking a carcinoma of the recto-sigmoid or the lower sigmoid which has already become adhered to and invaded the bladder. I wish to emphasize Dr. Jones's remark that certainly one of the most important phases in the removal of a cancer of this portion of the genito-enterologic tract is the adequate preparatory period, which has now become a rather routine custom in this country. I believe that some of the mortality from our colleagues of the continent would be avoided if they indulged in a little more preliminary preparation before operation was taken.

## MARRIAGE AMONG MENTAL DEFECTIVES

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BOSTON  
AND

LLOYD H. ZIEGLER, M.D.

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Among average or superior members of society, marriage presupposes adaptations and creates problems of a varied nature. It is difficult for all these to be satisfactorily resolved, even with every aid that can be brought to bear on them. In the case of handicapped persons who marry, the problems that ensue are no less numerous or complicated. But among the feeble-minded the awareness of such problems, by the nature of the circumstances, is relatively defective, and the burden of solution must be assumed largely by others in society more capable of bearing them.

This study was suggested by the admission of a woman to the public obstetric service of a large hospital. The facts pertaining to her are neither new nor unique. Doubtless similar persons can be found in any community. Her history follows:

*Hospitalization.*—Mrs. Q., a woman aged 20, was admitted to the indigent obstetric service June 19, 1935, at term, in her third pregnancy, which was normal. The children of two previous pregnancies had died soon after birth. Delivery of a male child weighing 7 pounds 14 ounces (3,573 Gm.) was spontaneous. The patient remained in the hospital fourteen days on a permit financed by the welfare department of the city. Her recovery was uneventful, except that it was noticed that she was uninterested in her environment and was unresponsive to instructions given by her attending physician for the care of herself and the baby. These features were so impressive that psychiatric consultation was obtained. The psychiatrist found that, according to the Stanford revision of the Simon-Binet intelligence test, her intellectual growth had been arrested when she was 7 years and 1 month old. Her basal mental age was in reality but 6 years. The intelligence quotient was 44. She did not know the meaning of Easter or the Fourth of July.

*Family.*—Such observations naturally aroused curiosity about her family. The patient's father had died of tuberculosis. Little more could be learned about him. The patient's mother, aged 51, lived with the patient and was usually dressed in filthy,

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From the Department of Gynecology and Obstetrics and the Department of Neurology and Psychiatry of the Albany Hospital and the Albany Medical College, Albany, N. Y.

ragged clothes. Her intellectual growth had become arrested at 8 years 4 months, according to the Stanford revision of the Simon-Binet test. She had been married twice and had been pregnant nine times; six children survived. Two of these were the patient and her identical (monozygotic) twin sister, whose intellectual growth was arrested at 6 years 10 months. It was also said that none of the other four children could read or write or do more than simple labor at irregular intervals. By further investigation it was learned that the living conditions of the brothers and sisters were little if any better than those of the patient. Petty crimes had been committed by some members of the family.

**Past History.**—The patient's past history has been obscured by the absence of intelligent observation and potent memory. She had gone to school a short time but had not learned to read or write. She and her twin sister had had speech defects from an early age. The patient was legally married at 17 by a clergyman to the son of a junk collector whom she had known but a few days. The reason given for such a hasty marriage was that she wished to show her twin sister, who had married five days earlier, that she could "catch a feller, too." Her husband, about ten years her senior, was regarded as a shiftless, incompetent laborer, known to use liquor to excess. He had been the recipient of some form of public or private relief almost continuously since his marriage. He had been known to sell welfare food orders to buy liquor.

**Home Conditions.**—The visit of a social worker to the patient's home revealed almost unspeakable conditions. The family had moved frequently, being evicted for nonpayment of rent. At the time of the visit, several months after the patient had left the hospital, they were living in the poorest section of the city on the top floor of a very rundown three story frame house facing the railway tracks. The three room apartment was sparsely equipped with old and broken furniture; in fact, one room contained no furniture whatever. The rooms were filthy and disorderly. The floor was covered with ashes and sticks of wood. The only bed present had a soiled mattress and a grimy old blanket. Burlap sacks were used as pillows. The dining table was covered with old potato peelings. A few dishes and kitchen utensils were scattered about. The apartment was nearly as cold as the winter weather outdoors.

**Follow Up.**—The social service follow up of the patient and her family is a sordid tale of hardship and poverty. Her husband worked but little, becoming intoxicated whenever

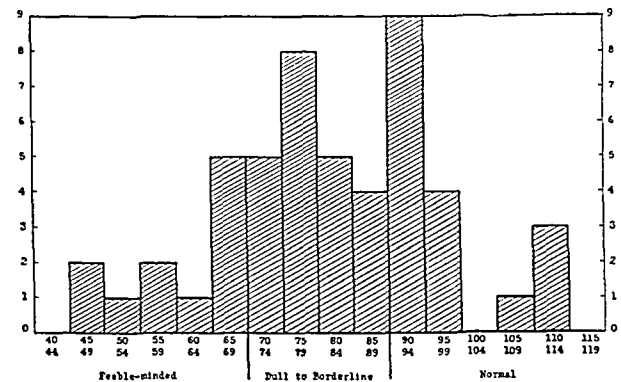


Chart 1.—Distribution of patients according to their intelligence quotients.

possible, at which times he was cruel and quarrelsome. The entire family suffered from undernourishment, insufficient clothing and cold. The baby died at 7 months of age as a result of injuries sustained from inhumane treatment during a drinking debauch of its father.. The patient was four months pregnant at the time of the death of the child. The fourth child has since been born in the hospital, and the mother and baby are being observed in the free clinic. The needs of the family are met by the city welfare department. Between 1932 and 1936 the patient's family and her nearest relatives were granted in excess of \$9,000 for relief and hospitalization.

In perusing the records of the hospital it was not difficult to find many others in the files of the obstetric department not unlike that of Mrs. Q. This fact prompted the study of fifty unselected married patients seen in the free antepartum clinic over a period of about four months between July and October 1936. The Stanford revision of the Simon-Binet test was given to these patients by an experienced psychologist. The results of this study are recorded in chart 1 and

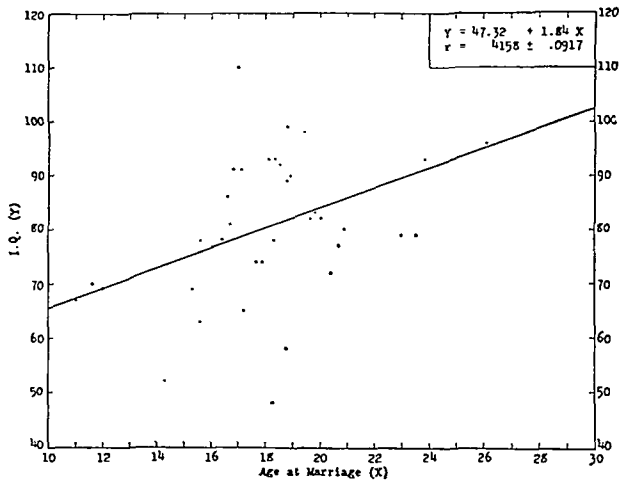


Chart 2.—Intercorrelation between age at marriage and intelligence quotient.

the table. The distribution of intelligence quotients approximates a normal curve in outline, suggesting random selection of the patients investigated. According to the tests, 22 per cent of these married women were feeble-minded, which is a far greater percentage than is to be found in the general population. In reality, they have participated in a form of child marriage, usually with governmental and religious sanction, that constitutes a more hazardous factor to society than the occasional child marriages so much publicized recently. And because of these marriages in our country, among persons imprisoned in a perpetual and unchanging childhood, it ill becomes us to cast the first stone at Mother India.

The intelligence quotients were plotted against age at marriage, as indicated in chart 2. This chart demonstrates, in general, that the lower the intelligence quotient the earlier they tended to marry.

In recent years the declining birth rate has attracted considerable attention. In order to learn something about pregnancy rates, the records of 964 obstetric patients who were delivered at the Albany Hospital in the years 1931-1935 were analyzed. Two hundred and sixty-two of these patients were confined in the maternity division supported by public funds. The remainder were able to pay for their own hospital care. The average number of months of exposure to pregnancy between pregnancies was 12.5 for the indigent group, in contradistinction to 22.4 for the self-supporting group, thus demonstrating a marked difference in the procreativeness of the two groups.

Perhaps of equal significance with birth rate is the survival rate of the children. In the case of the indigent group, the infant mortality was 94.6 per thousand live births, whereas for the self-supporting group it was 40.9. An analysis was made of the number of infants surviving the first year of life. A thousand pregnancies

in the indigent group produce 772 infants 1 year old, while a thousand pregnancies in the self-sustaining group produce 861 surviving infants. How well the children of these two groups may survive into the future is a problem, although it is known that the death rate among idiots and imbeciles is much higher than it is among normal people.

From such a survey we were led to consider the statutory impediments which the various states have enacted to prevent marriage among persons with outspoken arrests in psychic development. Such statutes vary enormously, as one would suspect, and include reference to psychoses and other diseases which are regarded as disqualifying for marriage.

The actual, or chronological, age of legal consent to marry is not uniform. The upper and lower age limits are 16 and 21 years for the female in Tennessee and Connecticut, respectively. There are modifications for these limits in all states to meet emergent obligations and to comply with the consent of guardians. Most states with

*An Analysis of Fifty Routine Antepartum Clinic Patients  
Investigated by the Stanford Revision of the  
Simon-Binet Test*

Chronological Age:	
Range.....	16 yrs.-43 yrs., 11 mos.
Median.....	24 yrs., 10 mos.
Intelligence Quotient:	
Range.....	0.46-1.13
Median.....	0.81
q <sup>1</sup> .....	0.715
q <sup>2</sup> .....	0.81
q <sup>3</sup> .....	0.925
Mental Age:	
Range.....	88-217 mos.
Mean.....	156.1 mos.
Median.....	12 yrs., 11 mos.
q <sup>1</sup> .....	11 yrs., 5 mos.
q <sup>2</sup> .....	12 yrs., 11 mos.
q <sup>3</sup> .....	14 yrs., 8 mos.
Standard deviation from mental age..	
29.37	

decrees prohibiting marriage among the feeble-minded provide for the withholding of the marriage license by the town or city clerk or other authorized person if he is aware that either party is legally incompetent to marry. In New York State a clerk who issues a license to marry to persons not competent, without first requiring them to make an affidavit showing that they are legally competent, shall be guilty of a misdemeanor. In the same state it is a misdemeanor to solemnize marriage if it is known that either of the parties is under the age of consent or is insane or an idiot, but the domestic relations law of New York permits the clergyman or officer, without such knowledge of legal incompetence, to solemnize matrimony legally once the license has been issued. In a number of states the applicant for a marriage license must make affidavit that he is free from the aforementioned defects.

In the District of Columbia and in nineteen states feeble-minded persons are not prohibited from marrying, although in some of these states the marriage may subsequently be declared void by judicial decree if one of the parties is an idiot or insane.<sup>1</sup> Twenty-nine of the states have laws attempting to cope with the problem. Perhaps the simplest is the Illinois law, which states that "no insane person or idiot shall be capable of contracting marriage." Massachusetts requires the certification of mental defect or disease in an institution to

1. Feeble-mindedness is very different from a psychosis, which may occur in persons of superior ability. Insanity is a legal term implying lack of responsibility sometimes associated with these disorders.

prohibit marriage. In Iowa the state board of control supplies quarterly to clerks of the court a list of such certified defectives who are disqualified for marriage. The clerk must refer to the list to be sure not to grant a license to a disqualified person. North Dakota requires an affidavit from a duly licensed physician showing that the contracting parties are not feeble-minded or otherwise disqualified. The North Carolina law defines the nature of the physician's duty in so certifying to the competence to marry, and false statement is a misdemeanor.

Many states prohibit clergymen or other officers from solemnizing marriage if it is known to them that either party is feeble-minded or has other disqualifying conditions. In Virginia any one having knowledge of such disqualifying attributes may appear before the clerk or clergyman and give reason why the marriage should not be consummated. In New Hampshire such questionable issues are referred to the state board of health.

Most states fail to acknowledge that marriage may entail the support of a family. In this respect the Indiana law (section 44-207) is unique and deserves being quoted:

No license to marry shall be issued where either of the contracting parties is an imbecile, epileptic, or of unsound mind, or under guardianship as a person of unsound mind, nor to a male person who is or has been within five years an inmate of any county asylum or home for indigent persons, unless it satisfactorily appears that the cause of such condition has been removed and that such male applicant is able to support a family and likely to so continue.

#### COMMENT

From our observations, and those of others, it seems clear that the feeble-minded above the grade of idiot may marry without much restraint even in states that have laws disqualifying them. The feeble-minded tend to marry earlier than normal adults and apparently they procreate more rapidly.

Our patient, Mrs. Q., was allowed to participate in a marriage contract without being sufficiently investigated. Her responsibility for entering into any kind of a contract is questionable. Her inability to care for herself, or even to learn to do so, is obvious. Her attempts to make a respectable home have been as feeble as her intellectual capacities. Children were born. Assuming that they were not feeble-minded on a hereditary basis, growth to adulthood in the environment which this mother provides would have a markedly adverse effect in fitting them to live in a cooperative community. On the other hand, if her children were feeble-minded—and this is the greater likelihood—they would perhaps suffer less harm from their home environment than those of normal intelligence but would nevertheless be deprived of the basic training and care so essential to the adaptations of the feeble-minded. It seemed natural for Mrs. Q.'s neighbors to be critical of her inadequacies. In the light of her definite arrest of psychic development, it is clear that her critics were neither understanding nor constructive in their condemnations.

One is impressed by the efforts of relief agencies who, with the best of intentions, pour out aid in such situations—firmly conditioned by incontrovertible facts—thus perpetuating them without much amelioration. This brings us to a consideration of the laws that have been intended to cope with such problems.

Unfortunately, law makers are not always biologists and therefore may not be sufficiently conversant with

conditions they aim to modify or control. Laws not infrequently mention idiocy (mental age 0 to 3 years) as a condition disqualifying for marriage. Few, if any, idiots are capable of attempting to contract marriage or to reproduce. Arrests of psychic development above this level (imbecility, with mental ages 3 to 7, and moronism, with mental ages 7 to 12) are frequently not mentioned in marriage-disqualifying laws. Most of such defectives are by nature incapable of, and irresponsible for, making contracts such as marriage. Since they often appear to be normal adults—but in reality are mere children—they are taken advantage of and exploited. In difficult times and in environments where they are not understood (and they usually are not) there is little recourse for many of them except in delinquency, relief rolls, or starvation.

Feeble-mindedness is a biologic condition, or state, with many possible causes. Heredity plays a considerable part in the transmission of this disease entity when it is not caused by injury or infection of the brain. It deserves to be classified with other diseases. It seems to be no minor defect in our marriage laws that they should in many instances be so worded as to place the responsibility for the recognition of this disease on a clerk, on a clergyman without medical training or on the defective himself. As a matter of fact, only a small percentage of physicians have had the training and experience to administer the tests by which feeble-mindedness above the very lowest grades may be recognized.

Governments have not attached sufficient importance to the age at which intellectual growth ceases; this is of much greater significance than the actual age of the person. If one examines the inmates of prisons, almshouses or reformatories, people on relief rolls or women who give birth to children out of wedlock, one finds that a far larger percentage of persons is included whose psychic arrest has occurred in childhood than is found in the population as a whole, in which the incidence of feeble-mindedness is about 4 per thousand inhabitants.

Sterilization has been advocated as a means of removing effectually the feeble-minded from the race. While students of the subject realize that the widespread use of this device can work but slowly, and perhaps ultimately ineffectually, nevertheless it may be applied to certain individuals to enable them to defend themselves from responsibilities which they are ill fitted to carry. A number of states have passed laws relating to the sterilization of defectives. In 1927 the United States Supreme Court upheld the validity of the Virginia sterilization law. Justice Holmes, in rendering the report, said:

We have seen more than once that the public welfare may call upon the best citizens for their lives. It would be strange if it could not call upon those who already sap the strength of the state for these lesser sacrifices, often not felt to be such by those concerned, in order to prevent our being swamped with incompetents. It is better for all the world, if instead of waiting to execute degenerate offspring for crime, or to let them starve for their imbecility, society can prevent those who are manifestly unfit from continuing their kind. The principle that sustains compulsory vaccination is broad enough to cover the cutting of the fallopian tubes. . . . Three generations of imbeciles are enough.

Segregation, with suitable vocational training, will do much to enrich the lives of some of these less fortunate people. At the same time, the social hazards of reproduction in this group can be eliminated. This

has never been adequately tried. If the costs of relief, dependence, delinquency and disease attributable to the feeble-minded could be transferred to the ledger on the side of wise segregation and training, not only would there likely be a definite and immediate pecuniary saving but there would also be future dividends of humanitarianism and prevention.

Compulsory registration of the feeble-minded is another way of attempting to deal with the problem. Reporting should be done to a central office, such as the department of mental hygiene or the department of health. Only those found by qualified examiners to have intelligence quotients of 70 or less should be registered. In this way the following of defectives and typhoid carriers would have much in common. Detection of persons with arrest of psychic development should begin in the public and private elementary schools. School officials could cooperate best by selecting for special study students who are retarded in their progress from grade to grade and those of school age who, by reason of their mental deficiency, have never been able to attend school. The wise utilization of knowledge about registrants might be vested in the authority of a commission having extensive knowledge and experience with such persons. Lists of registrants and consultation privileges with the special commission should be available to clerks and clergymen responsible for the licensure and solemnization of marriage. Under such circumstances, laws disqualifying the feeble-minded for marriage might be enforced more effectively. Courts should also have access to the same service. Too frequently courts sentence offenders in accordance with a legally specified prison term when, in reality, an unchangeable biologic condition exists, unameliorated by prison experience; from such persons the safety of society requires perpetual segregation. No single plan, or any combination of several methods, can be perfect. Such a commission, however, could utilize registration, wise guidance and supervision, sterilization and segregation, depending on the situation, in the most practical ways to discourage or prevent reproduction and antisocial living.

The expenditures incurred in the United States by allowing the feeble-minded to live as they wish, with palliative assistance, has perhaps been one of the heavy prices we have paid for what we call personal freedom. We are at the threshold of a reappraisal of the liabilities and the assets involved which can come about through a broadened interest in the public health. If individual liberty is lost when one has smallpox or leprosy, it would seem that the chronic disease feeble-mindedness might be controlled in the interest not only of the patients themselves but for the health, economy and safety of the public as well.

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#### ABSTRACT OF DISCUSSION

DR. DWIGHT L. WILBUR, San Francisco: The authors have raised some questions with regard to problems which will vitally affect our future. I agree that further study should be made of the problem of marriage among those who are mentally defective with the idea of reappraising the liabilities and assets of such marriages to the public health. There is still much controversy with regard to the influence of heredity on the mental equipment of the offspring and with regard to the effectiveness of sterilization of mentally defective persons in controlling the incidence of mental deficiencies. Since the problem has legal and sociologic implications, it seems that it would be wise to have more data available before addressing methods of



control of this problem to the courts and to sociologists and social workers. It should be recalled how difficult it has been to obtain enforcement by legal means and acceptance by the public of such well established methods of public health control as vaccination to prevent smallpox and as antitoxin in the prevention and treatment of diphtheria. Of equal importance to a study of the effect of hereditary influences and of sterilization in the control of feeble-mindedness and of other types of mental deficiency is a study of the influence of environment on the offspring of normal and of mentally defective persons. Such a study should be made before a definite policy is established with regard to the methods of dealing with this problem. Until further studies of the effect of heredity and environment on the development of mentally abnormal persons are available and lead to fairly definite conclusions, it would be wise for us to assume a rather conservative attitude in adopting an aggressive policy with regard to the best method of handling the problem of marriage among mentally defective persons.

DR. LAWRENCE KOLB, Lexington, Ky.: The authors are to be commended for bringing to attention in a striking way the folly and danger of unrestricted breeding of the unfit. It has become the fashion these days to scoff at measures designed to improve the race or to prevent its deterioration. The statistically minded tell us that if all the feeble-minded were sterilized there would be no definite decrease in the total number in the next generation, and unfounded statements are made that if eugenicists had had their way such and such a genius would never have been born. Breeding psychopaths and other defectives on the chance that one of them might turn out to be a genius is much like sowing weeds in a corn field with the hope that one may bloom into a beautiful flower. In any event, whatever might be said for the psychopath as a source of genius surely does not apply to the feeble-minded. The authors show that 22 per cent of their indigent groups of pregnant women were mentally defective according to accepted methods of testing, that the lower the intelligence quotient the earlier they tend to marry, and that the birth rate among the indigent is higher than among self-supporting more intelligent groups. We may rest assured that the innate selfishness common to all groups will prompt the more intelligent to disregard the unfavorable birth trend so far as it applies to their own personal convenience, while the morons, through unintelligent indifference to anything but animal needs, will continue to breed at a high rate. The remedy then lies in some positive action by the intelligent group. A start has been made through the medium of certain state laws, but these laws are, as a rule, ineffective, owing in part to the indifference or lack of sympathy of the public. The public must be aroused to the dangers in the present situation and the possibilities of improving it through measures that will take account of the defects inherent in intelligence testing and which will not interfere with the normal sexual urges of any one. The authors have given a broad outline of how the problem should be approached, but the public must be further educated before adequate remedies can be applied.

DR. FRED O. BUTLER, Eldridge, Calif.: Our experience in California is worthy of mention at this time. Perhaps some are not aware of the extent of sterilization that has been done in California, especially at Pacific Colony and Sonoma State Home, the two institutions for defectives in this state. We have sterilized to date over 12,000 mentally defective and insane, over 3,300 of this number at the Sonoma State Home, and of this number about 400 are married and getting along satisfactorily. We feel that without sterilization our marriages would not be so successful, when it is considered that they come from families with as many as twenty-three defectives in one family and the next largest family having seventeen defectives, both parents also being defective and likewise the grandparents. We have several of three generations in our institution and only one instance in which the offspring of these defective parents has been brighter than the parents, the majority of them having been far lower mentally than the parents. The average intelligence quotient of those married is about 60. Their marriages are about 100 per cent more successful than the marriages among the group presented here today, partly because of the careful investigating and the approving of the marriages. I feel that we do this more thoroughly than is done by the average

normal parents with their own sons and daughters because we feel a responsibility in allowing these boys and girls to marry. We ascribe our success to thorough investigation by the psychiatric social service department and keeping them under close supervision for about two years. Many of them have their own homes and they fit into communities far better than many so-called normal people. This could not, of course, be done so successfully without the operation for sterilization, which prevents a burdensome family on their hands. We have many come into our institution, the family having been broken up on account of their inability to care for their children.

## CANCER OF THE LARYNX

CHEVALIER JACKSON, M.D.

AND

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PHILADELPHIA

The literature of malignant disease of the larynx is so voluminous that any presentation should have a bearing only on the as yet inconclusively determined phases of the subject, especially those that seem to call for revision of opinion.

We have therefore analyzed our data with a view to determining what light they throw on the following questions:

1. Is the physician justified in limiting the use of irradiation to cases in which operation is contraindicated?
2. Where shall the line be drawn between cases for operation and cases for irradiation?
3. What is the bearing of the degree of malignancy on the choice between operation and irradiation?
4. Is it justifiable to do a laryngectomy for a small growth in the anterior commissure even if the degree of malignancy is high?
5. In view of the later improvements in the technic of irradiation is the surgeon not justified in doing fewer laryngectomies?

### 1. IS THE PHYSICIAN JUSTIFIED IN LIMITING THE USE OF IRRADIATION TO CASES IN WHICH OPERATION IS CONTRAINDICATED?

Our statistics show that up to the year 1930 the results of irradiation were so disappointing that, unquestionably, no patient with a growth of the class regarded as operable should have taken the practically hopeless chance of even relative cure by irradiation. Since the year 1930, however, our observations have led us to believe that there are growths classed as operable for which the patient is justified in choosing irradiation in preference to operation. The year 1930 was selected as the dividing line somewhat arbitrarily for convenience in studying our statistics. It should not be inferred that there was an abrupt change in our results or our opinion. In fact there is so much overlapping in the clinical evidence that a dividing line could not be clearly determined, and the evidence does not yet warrant a conclusive opinion. But the contrast afforded by the grouping of cases observed before and after the date mentioned has yielded a basis for present guidance in selecting the form of treatment that seems best for each particular patient.

Our statistics do not as yet justify abandonment of the well established operation of laryngofissure when the

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growth is operable by this method. By operable growth in this connection we mean early intrinsic cancer of limited extent.

On the other hand, when the malignant growth is locally ideal for operation but the patient is a bleeder or has a serious organic ailment such as marked arteriosclerosis, advanced cardiac disease, intractable diabetes, pulmonary tuberculosis, a psychosis, or any other condition abnormally shortening life expectancy, we would now class the patient as unsuitable for operation whereas formerly we would have advised operation. In other words, though we still feel that we should limit irradiation to the class of patients unsuitable for operation, classification of patients has been somewhat changed by the improved results obtainable by irradiation and we now classify as unsuitable for operation a somewhat larger proportion of patients with early intrinsic disease.

Table 2 shows data from our records bearing on the question of irradiation in the treatment of cancer of the larynx.

Terminal records are incomplete. So far as can now be determined no patient survived a year after the

TABLE 1.—General Data on a Series of 631 Cases of Malignant Disease of the Larynx Observed Prior to 1930

(Patient seen in consultation, records incomplete; biopsies, operations and irradiation done elsewhere, or patient untreated, 262)	
Age: youngest male, 18; youngest female, 24; 20-30, 6; 30-40, 32; 40-50, 68; 50-60, 123; 60-70, 34; 70-80, 51; 80-90, 6; uncertain, 52 (some of the ages estimated)	
Sex: female 35, male 335, unrecorded 1	
Histologic report: squamous carcinoma 343; basal cell carcinoma 4; glandular carcinoma 2; endothelioma 3; sarcoma 4; lymphoma 4; osteoma 2; osteosarcoma 2; chondroma (malignant) 3; angioma (malignant) 1; leiomyoma (malignant) 1	
Treatment by laryngofissure.....	111
Treatment by laryngectomy.....	97
Treatment by irradiation.....	106
Patient did not return for treatment.....	55
	369

beginning of the irradiation. All the patients were deemed unsuitable for operation for local or general reasons. Three patients with positive serologic reactions had energetic antisyphilitic treatment before irradiation was begun. Many of the patients in this series were seen in consultation and were not followed through the treatment.

The results of irradiation in the foregoing series of cases were so discouraging that they were regarded as justifying advice against irradiation even when the growth is inoperable. Radiation as then applied if used in sufficient strength to get any effect seemed to hasten rather than retard a fatal termination. It should be stated, however, that in many of the cases metastases had rendered the prognosis utterly hopeless before irradiation was used.

In 1930 and the two subsequent years unquestionable evidence of better results from irradiation, especially the results from the use of radium in the hands of Dr. George E. Pfahler, convinced us that improved technic rendered irradiation advisable in all cases in which the cancer was inoperable and there was no evidence of pulmonary metastases or general carcinomatosis.

Then came the technic of irradiation with the roentgen ray devised by Coutard. The results of the application of the roentgen ray and of radium by the newer technics have been so good that we have since advised

irradiation in all cases in which the cancer is inoperable, but we have left to the judgment of the radiologist in charge the choice between the use of radium, of the roentgen ray and of the two combined. In the cases reported in our records irradiation has been performed by Drs. M. C. Cameron, Russell H. Boggs, William S. Newcomet, George E. Pfahler, Henry K. Pancoast.

TABLE 2.—Patients with Malignant Disease of the Larynx Treated with Radiation Prior to 1930

Number of patients.....	166
Female .....	11
Male .....	94
Sex not recorded.....	1
Result on growth not recorded.....	13
Growth not arrested.....	49
Growth arrested .....	44
Recurrence after arrest.....	44
Serious complications attributable to irradiation, perichondritis, chondral necrosis, extensive sloughing, secondary reaction, delayed reaction .....	32

W. Edward Chamberlain, Eugene Prendergrass, Willis F. Manges, John T. Farrell, Karl Kornblum, Leon Solis-Cohen, J. Gershon Cohen and their associates.

Complete data on all the patients subjected to irradiation since 1930 will be published later. During this period excellent results were obtained in a number of cases by Dr. W. Edward Chamberlain using a modified Coutard technic:

The patient receives 125 roentgens daily to each side of the larynx for twenty-five treatments, a skin portal from 7 to 10 cm. in diameter and a skin target distance of 50 cm. being used. With the factors 180 kilovolts (average), 8 milliamperes and a filtration of 2 mm. of copper plus 1 mm. of aluminum, 10.6 roentgens a minute is delivered to the skin, the time being 11.8 minutes to each side. The total dose is 3,000 roentgens or slightly more to each side.

The data shown in table 3 seem to justify our decision in favor of irradiation, at least for cases in which the cancer is inoperable.

TABLE 3.—Data on Patients with Inoperable Malignant Disease of the Larynx Since 1930

Number of patients.....	17
Female .....	1
Male .....	16
Growth not arrested.....	1
Growth arrested .....	16
Recurrence after arrest.....	7
Serious complications attributed to irradiation (perichondritis, chondral necrosis) recorded .....	1
Death within 1 year of intercurrent diseases without local recurrence..	2
Death within 1 year of cancer of larynx or vicinity.....	3
Patient living, free from recurrence after 3 years.....	4

The cancer in all cases was deemed inoperable because of (a) extent of the lesion, (b) adenopathy, (c) extrinsic location or (d) involvement of the posterior portion of the tongue. Considering the unfavorable character of the lesions, the results are remarkable.

In answer to the question Is the physician justified in limiting the use of irradiation to cases in which operation is contraindicated? we may say that deduction from our statistics has led us to believe that he is scarcely so justified, but we still believe that, for the present, laryngofissure should be preferred to irradiation in cases of early intrinsic cancer. We believe also

that there are cases in which total laryngectomy may still be regarded as the treatment of choice. The indications for laryngectomy have recently been very clearly stated by Schall,<sup>1</sup> who has also shown convincing proof of the excellent psychic and social adjustment made by most of the patients despite the mutilating and crippling character of the operation.

## 2. WHERE SHALL THE LINE BE DRAWN BETWEEN CASES FOR OPERATION AND CASES FOR IRRADIATION?

Fundamental to the consideration of the choice between operation and irradiation is a clear statement of what is meant by operation. There are four classes of operation, each so different as to both the operative risk and the after-condition of the patient that to take all four classes as one method for comparison with irradiation would be very misleading. We shall therefore consider (a) endoscopic operation, (b) laryngofissure, (c) laryngectomy and (d) lateral pharyngotomy.

With both endoscopic operation and laryngofissure the operative risk is negligible and the after-condition

three recurrences. Kernan's conclusion is the same as ours, that while endoscopic removal is possible it is not to be recommended.

The tip of the epiglottis is the only part of the extrinsic area that, according to our experience, is amenable to operation, and this in only one class of case.

Nowhere in the body is there a greater contrast between the early and the late stages than in the epiglottis. Though our cases of cancer in the early stage were few, they show that a small and extremely early carcinoma located at the center of the tip of the epiglottis is, for a time at least, a strictly local process so amenable to surgical treatment that direct laryngoscopic extirpation can be curative. By way of contrast, a lesion that has started or has extended slightly downward becomes one of the most fatal of all carcinomas of the larynx, because of leakage into the base of the tongue.

New<sup>3</sup> has on several occasions, notably in a cancer symposium at the Clinical Congress of the College of

TABLE 4.—Cancer of the Epiglottis

Case	Sex	Age	Location	Irradiation	Tracheotomy	Other Treatment	Result	Histologic Report	Comment
1	♂	42	Tip of epiglottis, central	.....	.....	Endoscopic	Patient living, well 9 years later	Squamous carcinoma	Before days of typing
2	♂	31	Tip of epiglottis, central	.....	.....	Endoscopic	Patient living, well 5 years later	Squamous carcinoma	Before days of typing
3	♂	54	Tip of epiglottis, left margin	For recurrence	Palliative in later stages	Endoscopic amputation; lateral pharyngotomy for recurrence	Recurrence, tongue; death 1 year later from pulmonary carcinoma	Squamous carcinoma	Before days of typing; clinically aggressive
4	♂	61	Right margin	For recurrence	Palliative in later stages	Endoscopic amputation; lateral pharyngotomy for recurrence	Recurrence, tongue; death 1½ years later from mediastinal metastases	Squamous carcinoma	Before days of typing; clinically aggressive
5	♀	42	Tip of epiglottis, central margin	.....	.....	Endoscopic amputation	Patient living, well 2 years later	Squamous carcinoma, grade 2	

of the patient is practically normal. With both laryngectomy and lateral pharyngotomy the operative risk must be considered and the after-condition of the patient is one of mutilation and economic disability. These disadvantages do not mean that these operations are inadvisable, but the distinctions are essential to an unprejudiced consideration of the choice between operative and irradiative treatment.

**Endoscopic Operation.**—We have seen a number of instances in which removal of material for biopsy had so completely removed the growth that no evidence of a malignant process could be found in the mass of basal tissue removed at subsequent laryngofissure. This, however, has not led us to feel justified in endoscopic excision except in certain cases of epiglottic cancer.

Kernan<sup>2</sup> stated in a recent paper that he had had two cases in which the tumor had been completely removed endoscopically when tissue was taken for biopsy. In one of his cases no further procedure was done; in the other the cord was removed by laryngofissure. In neither case was there a recurrence. According to Kernan, Lynch had reported nine cases of endoscopic removal of a laryngeal carcinoma with

Surgeons, held in San Francisco three years ago, advocated the extirpation of small tumors of the epiglottis of low grade malignancy by surgical diathermy under suspension laryngoscopy. Tucker<sup>4</sup> has reported cases of epiglottic tumor in which he removed the involved epiglottis by the laryngofissure route.

In view of the foregoing facts, we may say that our clinical experience seems to indicate that in the case of cancer of the epiglottis the line between operation and irradiation is to be drawn between the small, extremely early lesion located centrally on the tip, which is an operable lesion, and a growth below the margin by origin or extension, which is of questionable operability. For all growths of the latter class irradiation is our first choice.

**Laryngofissure.**—For a small, early growth located within the intrinsic area in a patient otherwise free from organic disease we would not feel justified in advising anything other than laryngofissure. On the other hand, for a patient with such a growth whose life expectancy is seriously shortened by diabetes, pulmonary tuberculosis, cardiovascular disease or other organic disease we would advise irradiation. It cannot

1. Schall, Leroy A.: Laryngectomy, Its Place in the Treatment of Laryngeal Cancer, *Pennsylvania M. J.* 41: 261-267 (Jan.) 1938.  
2. Kernan, John Devereux: A Critique of the Treatment of Laryngeal Cancer, *Laryngoscope* 48: 295-301 (May) 1938.

3. New, Gordon B., and Figg, Frederick A.: Treatment of Carcinoma of the Larynx, Surg., Gynec. & Obst. 62: 420-423 (Feb., No. 2A) 1936.  
4. Tucker, Gabriel: Cancer of the Epiglottis: Total Extirpation of the Epiglottis by the Laryngofissure Route, *Tr. Am. Laryng., A.* 57: 216-223, 1935.

be too strongly stated, however, that this preference for irradiation is not due to any operative risk; not one of the conditions mentioned, in a properly prepared patient, is a contraindication to laryngofissure. The preference is based on the fact that irradiation has now reached a degree of efficacy that renders it probable that the patient will live out his short expectancy without recurrence after irradiative arrest. The extent to which the conditions mentioned are to be regarded as contraindications to irradiation must be decided in the particular case.

Of all the cases of malignant disease of the larynx in which laryngofissure was performed prior to 1930 there are 111 that are sufficiently complete as to details to be worth analysis. These cases are divided into two groups for the purpose of determining the curability of malignant disease of the larynx by laryngofissure in cases suitable for this procedure. The question that immediately arises is Why do the operation in unsuitable cases? The reason is that when, in the days when irradiation was so disappointing, a patient with a cancer that was not ideal for laryngofissure refused to have a laryngectomy done, laryngofissure was the alternative. The responsibility was placed entirely on the patient. If, after full explanation of the increased risk of recurrence, the patient insisted on taking the increased risk rather than lose his larynx, it seemed inhuman to refuse to try to help him. A number of the patients were physicians. Under such circumstances it was deemed proper to do laryngofissure, but it would seem improper to include these cases in a group analyzed for the special purpose of determining the curability of cancer of the larynx by the laryngofissure route in suitable cases. This grouping enables the surgeon to tell future patients what the chances are in the class of case to which they belong. In no instance was laryngofissure done for advanced or extrinsic cancer when there was no hope of adequate removal. It may here be stated parenthetically that this situation is handled better today by advising patients who are not ideal subjects for laryngofissure (group A) to be treated with irradiation if they refuse consent to laryngectomy.

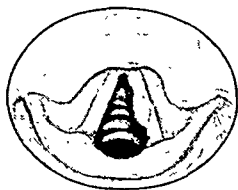


Fig. 1.—Small early cancer of the left cord, as seen reversed in the mirror. In this stage cancer is curable in 82 per cent of the cases, but unfortunately in all but 19 per cent it is overlooked. The only symptom is slight hoarseness, usually intermittent. Frequent or persistent hoarseness in an adult should be regarded as of cancerous origin until proved otherwise by proper diagnostic methods. Total laryngectomy would be a rare operation if all intrinsic laryngeal cancers were discovered in this stage.

In table 5 are included some cases (group A) in which laryngofissure was done although we had urged laryngectomy as preferable; the patient refused the latter and preferred to take the greater chance of recurrence involved in a laryngofissure for a lesion too extensive for best chances of success by this procedure. These cases are included here for completeness but should not be taken as criteria of the adequacy of laryngofissure in suitable cases. They were eliminated for this reason in a selected series of cases presented as part of the "Cancer Is Curable" symposium arranged by the late Franklin Martin.<sup>5</sup>

Insufficient time has elapsed for us to report finally on the results obtained in patients operated on since 1930, but it may be said that, of forty patients in whom

laryngofissure was done between 1930 and 1934, thirty-four, or 85 per cent, were free from recurrence three years after operation. This series includes all patients in whom this operation was done during the aforementioned period except one who died of cardiac disease before the lapse of three years. Several of the cases would be in the "unsuitable" group if such a division as was made in the tabulation of the cases in which operation was performed prior to 1930 were made in this series.

**Laryngectomy.**—As between laryngectomy and irradiation we are decreasing the number of laryngectomies in proportion to the number of patients treated with irradiation. We find irradiation better for many patients for whom a very few years ago we would have advised laryngectomy.

One class of case stands out sharply and clearly in our minds, namely that in which life expectancy is shortened by organic conditions independent of the laryngeal cancer. In such cases, it seems to us, irradiation should be used. Total laryngectomy should be reserved for the well preserved patient with a good vascular system for his years who is organically sound. There are some patients in whom no organic disease can be found who are nevertheless poor operative risks. We feel that the surgeon should beware especially of the patient who acknowledges "moderate drinking." Usually this admission means that, though perhaps rarely intoxicated, the patient drinks steadily all the time he is awake. For seventeen or eighteen hours out of each twenty-four his capillaries are dilated, his heart accelerated and his mental activity goaded. Such a patient, though not to be classed as an alcoholic addict, is a poor subject for laryngectomy. With a cancer of the larynx locally beyond the limit of laryngofissure yet still intrinsic, he will do better, on the average, with irradiation rather than with laryngectomy.

Table 6 presents data concerning the cases in which laryngectomy was done prior to 1930. In considering the rather high operative mortality one should make due allowance for the lack of the then undeveloped knowledge of diabetic control, edentulous preparation and other factors that increased the risks of major operations. Many of the operations were in cases of extensive local and metastatic lesions that would today in our opinion be classed as unsuitable for operation in the sense that operation is hopeless and irradiation hopeful. It should be noted that in only eighteen of the entire ninety-five cases the cancer was definitely intrinsic. Moreover, though degrees of malignant aggressiveness were recognized clinically,<sup>6</sup> pathologists had not developed the technic of

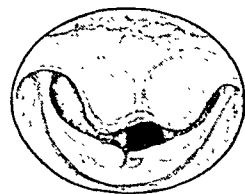


Fig. 2.—The overhanging epiglottis concealed from mirror view until late a cancer that started on the anterior end of the left cord. Visualization of the anterior commissure in all adults is necessary if cancer is to be detected in the curable stage. This visualization can be done in every patient with the direct laryngoscope.

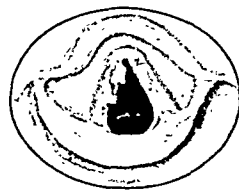


Fig. 3.—Leukoplakia of the larynx. In the larynx as elsewhere on mucosal surfaces, leukoplakia is potentially precancerous and should be extirpated.

5. Jackson, Chevalier: Cancer of the Larynx: Its Curability by Laryngofissure, Surg., Gynec. & Obst. 58: 431-432 (Feb. 15) 1934.

6. Jackson, Chevalier: Peroral Endoscopy and Laryngeal Surgery, St. Louis, Laryngoscope Company, 1915. (This book is out of print but is in most libraries. The French translation, entitled "Endoscopie et chirurgie du larynx," is still obtainable from the publisher, Gaston Doin & Cie, Paris.)

preoperative determination from biopsy specimens. The aggressiveness shown by the clinical progress of many of the patients indicates that a considerable number of them would not have been operated on under our criteria of today.

TABLE 5.—*Patients with Malignant Growths of the Larynx Operated on by the Laryngofissure Route Prior to 1930*

Group A: Laryngofissure (patient's choice) in cases not strictly suited to this procedure.....	51
Operative deaths .....	2
Untraceable patients .....	2
Deaths from cancer of the larynx before 3 years notwithstanding subsequent laryngectomy for recurrence.....	6
Deaths from cancer of the larynx before 3 years notwithstanding subsequent irradiation .....	6
Deaths from cancer of other regions.....	2
Deaths from disease other than cancer before lapse of 3 years.....	2
Patients living and free from recurrence at end of 3 years (of 23, 47 per cent).....	11
Group B: Laryngofissure in cases considered ideal for this procedure.....	80
Operative deaths .....	1
Untraceable patients .....	13
Deaths from cancer of the larynx notwithstanding subsequent laryngectomy .....	6
Deaths from cancer of the larynx notwithstanding subsequent irradiation .....	4
Deaths from cancer of other regions.....	2
Deaths from accident or disease other than cancer prior to end of 3 year period.....	2
Patients living and free from recurrence after 3 years (of 62, 80 per cent).....	50

Data on the seventy-eight cases in which laryngectomy was done since 1930 are not given here because they are not yet completely tabulated.

**Lateral Pharyngotomy.**—Any attempt to save the life of a patient otherwise doomed to death by malignant disease is not only justifiable but laudable. The percentage of success obtained by Orton<sup>6a</sup> and some other surgeons with extensive extirpations by the lateral route

TABLE 6.—*Patients Operated on by Total Laryngectomy Prior to 1930*

Number of patients.....	95
Operative deaths (within 30 days after operation, primary and secondary operations included; 9 per cent).....	9
Intrinsic cancer (too extensive for laryngofissure).....	18
Extrinsic cancer .....	77
Metastatic adenopathy .....	16
Pharynx or hypopharynx resected.....	18
Cervical esophagus resected.....	5
Tongue resected .....	3
Previous irradiation .....	3
Previous laryngofissure .....	4
Previous laryngectomy .....	8
Patient untraceable .....	11
Fatal recurrence .....	31
Deaths from intercurrent diseases .....	4
Deaths from "cancer" of other viscera, without local recurrence.....	6
Deaths from general carcinomatosis .....	7
Patients free from recurrence after 3 or more years (of 75 traceable patients surviving operation, 36 per cent).....	27
Patients surviving 3 years who had extrinsic cancer (27 traceable)....	6
Patients surviving 3 years who had intrinsic cancer too extensive for laryngofissure (of 27 traceable, 78 per cent).....	21

should encourage them to continue their efforts. There is no question as to the accessibility of the back wall of the larynx by this route, but our own early results were so discouraging and the recent results of irradiation have seemed so surprisingly good by comparison that we at present place party wall laryngeal cancers in the extrinsic class, for which irradiation is preferable to operation.

### 3. WHAT IS THE BEARING OF THE DEGREE OF MALIGNANCY ON THE CHOICE BETWEEN OPERATION AND IRRADIATION?

The question of the bearing of the degree of malignancy on the choice between operation and irradiation is of fundamental importance. It can, we believe, be answered definitely enough as to operation, but the question of irradiation is so interlocked with the matter of the relative radiosensitivity of the four types of malignant process now accepted by pathologists that, for the present at least, the decision must rest with the radiologist and the pathologist consulted in the particular case.

On the operative phase of the subject we may say that our experience has convinced us that the degree of aggressiveness in the particular case is of primary importance. Many years ago one of us pointed out the great variation in degrees of malignancy and its bearing on the results,<sup>6</sup> but until the formulation of histologic types by Broders we had no guiding criteria. Since our histologists have systematically typed our biopsy speci-

TABLE 7.—*Laryngofissure by the Anterior Commissure Operation*

Number of patients (traceable).....	34
Operative deaths .....	0
Recurrence within 1 year, requiring secondary laryngectomy; patient alive and well at end of 3 years.....	1
Recurrence treated by irradiation; death within 1 year.....	1
Deaths from cancer of the larynx and metastases.....	1
Deaths from malignant disease of other regions without local recurrence .....	1
Deaths from disease other than cancer, without recurrence.....	2
Deaths from accident .....	1
Patients free from recurrence at end of 3 years (79 per cent).....	27

mens we have based certain decisions as to choice of treatment on their reports.<sup>7</sup> Most of our clinical work in recent years has been based on the grading of Dr. Frank W. Konzelmann. There may in some cases be a variation in the histologic picture in different parts of a cancer; therefore for typing it is important that the histologist have an ample specimen. In the case of large growths we believe it best to take a specimen from two or more locations; in the case of small growths it is well to remove the entire tumor.

A number of years must elapse before definite rules can be laid down, but our experience so far has led us to formulate a general outline as follows:

(a) We deem laryngofissure advisable for every small early growth anywhere in the intrinsic area in a patient free from general organic disease regardless of the degree of malignant aggressiveness.

(b) For an advanced but still intrinsic growth of grade 1 or 2 in a patient free from other organic disease we would advise laryngectomy, but we would deem irradiation preferable for cancer of grade 3 or 4.

(c) For intrinsic growths with glandular metastases we deem irradiation preferable regardless of grading.

(d) In a general way it may be said that extrinsic growths are less amenable to operation and more amenable to irradiation as compared with intrinsic lesions. We are inclined at present to regard tumors of grade 4 as more sensitive but yielding results less permanent as compared with tumors of grade 1. Grades 2 and 3 are relatively similar but less sharply contrasted.

6a. Orton, J. Boylan: Cancer of the Larynx: Immediate and Ultimate Results in One Hundred Operative Cases, *Tr. Am. Laryngol. A.*, 1938.

7. Jackson, Chevalier, and Jackson, Chevalier L.: *The Larynx and Its Diseases*, Philadelphia, W. B. Saunders Company, 1937.

4. IS IT JUSTIFIABLE TO DO A LARYNGECTOMY FOR A SMALL MALIGNANT GROWTH IN THE ANTERIOR COMMISSURE?

It is universally accepted among surgeons that it is best, in dealing with a malignant tumor anywhere, to remove the growth with an adequate area of surrounding normal tissue without cutting into the neoplastic tissue.

The only question to be determined then, in the case of laryngeal cancer, is whether or not this can be done without extirpating the whole larynx. If the ordinary technic of laryngofissure is followed the clipping of the cartilage will certainly go right through a growth in the anterior commissure. This deplorable procedure can be entirely avoided in the case of small growths by the special anterior commissure technic which has been in use in our clinic twenty-one years.<sup>8</sup> Until three years ago this operation had been done for a small

In answer to the question Is it justifiable to do a laryngectomy for a small malignant growth in the anterior commissure? we may say that in our opinion this procedure is perfectly justifiable and proper if the surgeon's experience leads him to believe that in performing it he is acting for the best interest of the patient. In our own work, however, since the development of the anterior commissure operation, we have found that it is not necessary to sacrifice the whole larynx in such cases. It should be stated that before doing the anterior commissure operation we make certain in each case that the growth is small. Certainty is the result of systematic preoperative examination. Furthermore, we pay particular attention to the grade of malignancy in deciding between laryngofissure and laryngectomy and between operation and irradiation.

Before doing any operation for cancer of the larynx we wish to know the extent of the growth, the location

TABLE 8.—Long Histories of Tumors; Triple Primary Growths

Case	Age, First Tumor; Sex	Age, Last Tumor	Histologic Report, First Tumor	Treatment	Result	Interval, Years	Histologic Report, Second Tumor	Treatment	Result	Interval, Years	Histologic Report, Third Tumor	Treatment	Result	Comment
1	27, ♀	37	Papilloma	Excision	Apparent cure	3	Granuloma	Radium elsewhere	Apparent cure	5	Squamous carcinoma	Laryngectomy	Local, no recurrence; death from carcinoma of lung 11 years later	Total duration of history 21 years
2	About 6, ♀	49	Papilloma (?)	None	Apparent recovery	25	Edematous fibroma; papilloma	None	Apparent recovery	18	Basal carcinoma	Radium; tracheotomy	Death from carcinoma of larynx, mediastinum	History 43 years; 1 year after tracheotomy squamous carcinoma found
3	61, ♀	67	Fibroangioma	Excision	Cure	6	Squamous carcinoma, grade 2	Coutard series	Apparent cure	3	.....	.....	.....	Larynx and voice apparently normal after 3 years; benign-malignant sequence
4	21, ♂	39	Fibroma (soft)	Excision	Cure	7	Myxoma	Excision	Cure	11	Basal carcinoma	Roentgen; radium	No recurrence after 3 years	History 36 years; carcinoma cured (3 years), irradiation
5	22, ♂	49	Papilloma	Excision	Cure	11	Fibroma (hard)	Excision	Cure	16	Sarcoma	Laryngofissure	No recurrence after 3 years	History 27 years; cure of sarcoma by laryngofissure
6	36, ♀	52	Papilloma	Excision	Cure	9	Angioma (true)	Excision	Cure	7	Cylindric celi carcinoma, larynx; adenocarcinoma, mamma; squamous carcinoma, cervix uteri	Palliative tracheotomy	Death	History 16 years; triple primary growth; one in larynx rare

growth in the anterior commissure in forty-two cases, and of these thirty-four were traceable. Table 7 is a summary of the results.

Operative technic is not within the scope of this article, but there are two points that seem to require mention because they may have had a bearing on the results obtained and because, though described many years ago, they seem to have been ignored by writers and operators. One is the value of the anterior commissure operation described. The other is the rule that skin flaps should not be made and the larynx should not be even partially skeletonized in laryngofissure. The line of incision in the skin should be carried down to the cartilage layer by layer without any separate retraction. The abundance of soft tissue with vessels intact, undetached from the external perichondrium, preserves the vitality of the external perichondrium and thus prevents necrosis of the thyroid cartilage.

8. Jackson, Chevalier: The Results of Operative Methods in the Treatment of Cancer of the Larynx, Symposium, Ann. d. mal. de l'oreille, du larynx 41: 1221-1239, 1922.

of its lower border and whether or not there is evidence of leakage out of the laryngeal box. We feel it quite unnecessary for the surgeon to be so often astonished to find at operation a large extent of subglottic growth or an enlarged lymph node over the cricothyroid membrane. Both of these conditions can easily be and, we think, should be determined by preoperative examination. This consists of three procedures: direct laryngoscopic examination, external palpation and roentgen examination of the neck.

Before deciding to do an anterior commissure operation it is necessary to know that the growth really is small. Only too often what looks in the mirror like a small growth is found on direct laryngoscopic examination to be so extensive as to exclude all hope of adequate removal by laryngofissure. To do the anterior commissure operation would certainly be disappointing; the ordinary clipping laryngofissure would be worse still. This deplorable pitfall is entirely avoidable. The exact size of the growth and the precise location of its



lower border can almost always be determined by direct laryngoscopic examination of the subglottic region, and this is the only way in which the determination can be made beforehand. The best instrument for this examination is the rotating laryngoscope, though most of our work has been done with the standard anterior commissure form. In many cases what appears in the mirror to be a small growth at the anterior commissure is found to be a large subglottic lesion extending downward to the cricothyroid membrane, which always suggests possible leakage out into the soft tissues of the neck through the cricothyroid membrane or even between the cricoid and thyroid cartilages. Whether or not such leakage has occurred can often be determined by delicate palpation.

When we speak of the palpation of the larynx we do not refer to the routine, and of course necessary, surgical search for lymph nodes in the neck. We mean a careful and delicate outlining of all the laryngeal cartilages with the palpatory surface of the index finger trained to the contour of the normal. Any filling in or firmness of the normal slight depression between the thyroid and cricoid cartilages is a warning of probable leakage. The next step is to palpate every square centimeter of the cartilages for tenderness; if any tenderness is found, perichondritis is probable and any operation is contraindicated. Then a careful palpation of the region of the cricothyroid membrane is made for that little lymph node whose presence is so often a surprise at operation. It can always be detected at preoperative examination unless the neck is very fat. Of course the enlarged node found at operation may not show histologic evidence of carcinomatous metastasis, but we believe that the clinician is justified in advising against laryngofissure in most cases in which an enlarged gland has been found at preoperative examination.

The lateral roentgenogram is often valuable as a graphic representation of a laryngeal growth. It is of especial value when infiltration of the anterior subglottic region causes resistance to the direct laryngoscope. In such cases the process is beautifully delineated by the injection of a few cubic centimeters of iodized oil.<sup>9</sup> When this degree of infiltration is present the anterior commissure operation or any operation by the laryngofissure route is contraindicated.

##### 5. IN VIEW OF THE LATER IMPROVEMENTS IN THE TECHNIC OF IRRADIATION IS THE SURGEON NOT JUSTIFIED IN DOING FEWER LARYNGECTOMIES?

Elapsed time is not yet available in many of our cases because of the recency of development of the Coutard technic of roentgen irradiation and of the most efficient use of radium, but our experience is sufficient to warrant the belief that the future will probably see a progressive decrease in the relative number of laryngectomies.

One obvious reason for this is that, whereas formerly the surgeon was justified in taking desperate chances by laryngectomy when the patient's general expectancy was short, because of the 100 per cent mortality without treatment, the greatly increased efficiency of irradiation indicates that laryngectomy should now be limited to good surgical subjects of good general expectancy.

## ABSTRACT OF DISCUSSION

DR. MAX CUTLER, Chicago: The paper presented by the Jacksons is both valuable and comprehensive. The question of surgical intervention and irradiation in the treatment of carcinomas of the larynx involves three types of tumors: 1. Large, extensive, inoperable, extrinsic carcinomas of the larynx, which are outside the domain of surgical treatment but which, as a rule, are composed of highly undifferentiated cells and are radio-sensitive, require no discussion, as they are admittedly inoperable both technically and biologically. 2. At the other extreme are small carcinomas limited to the true vocal cord, which are technically operable. When biopsy discloses an adult hornifying squamous type and the lesion has not reached the anterior commissure, surgical removal gives excellent results and is the method of choice. About 20 per cent of the lesions, however, affect the true vocal cord and are technically operable but biologically inoperable. In spite of their small size and technical operability, they are composed of undifferentiated cells which have extended along the lymphatics anteriorly to the commissure or posteriorly to the arytenoid process. Surgical removal is commonly followed by local recurrence, and the surgeon is surprised to find a local recurrence after the removal of a lesion which seemed so favorable and so definitely operable. Such lesions are radiosensitive and respond well to radiation therapy. It would be interesting if, in surgical statistics, they were segregated and an attempt made to determine whether the failures do not occur when the tumor exhibits this structure. Perhaps the 20 per cent would respond better to irradiation. There are no statistics on irradiation, however, to support this thesis. 3. There exists an intermediate type, with which a decision between surgical treatment and irradiation is difficult. The difficulty may be due to the lesion's being of borderline operability or to the patient's age or his general condition, which may contraindicate operation. The individual factors in each case must be carefully considered. These factors are histologic and clinical. Histologically, if the tumor is highly undifferentiated, it is generally radiosensitive. If it is of an adult squamous form, it is generally radioresistant. A more accurate guide to radiosensitivity, however, is the fixation or mobility of the cord. The highly undifferentiated tumors are almost without exception movable even when they are extensive. The differentiated types are nearly always fixed. When a discrepancy exists between the structure and the mobility of the parts, the latter is the more reliable sign. It is important to recognize that fixation may be due not to neoplasia alone but also to inflammation. A moderate amount of irradiation invariably results in reestablishment of mobility when fixation is due to inflammation.

DR. SIMON JESBERG, Los Angeles: In 1931 Coutard presented his results covering a ten year period of treatment of laryngeal cancer by irradiation. Previously operation was considered the only hope for cure of this disease, at least in the United States. Surgical treatment has since been replaced more and more by irradiation. Selection of type of treatment is the important problem confronting the surgeon today. The bad results of a few years back have been much lessened by improved technic in irradiation, and the indications for surgical intervention have been curtailed as a consequence. Entire removal or destruction of a cancer is essential for a cure. Whatever method is selected, the good and the bad end results must be considered. Many factors besides the actual pathologic conditions, such as the age, occupation, physical and psychic status and economic position of the patient must be considered. For example, a radio announcer aged 42 had a small grade 3 squamous cell carcinoma just above the arytenoid process. Loss of voice would have been an economic catastrophe. Laryngofissure did not offer much chance for cure. As a result of irradiation he has a good voice and is able to keep his position. After three years there has been no recurrence. Slight dryness and huskiness of the voice are his only complaints. If he had had a neoplasm of a low degree of malignancy, the irradiation required would have given a much worse end result and probably less chance of cure than surgical intervention. As the efficiency of irradiation is developed there will be fewer operations. It is only by the study of such a large series as the authors' that one can

9. Jackson, Chevalier L.: The Value of Roentgenography of the Neck with Special Reference to Its Use in the Diagnosis and Treatment of Laryngeal and Tracheal Obstruction, *Ann. Otol., Rhin. & Laryng.* 45: 951 (Dec.) 1936.

learn to select the treatment intelligently. For a very small tumor of a high grade of malignancy in the anterior commissure, I would recommend surgical removal by laryngofissure followed by irradiation.

DR. JOSEPH C. BECK, Chicago: I am sorry Professor Coutard is not here to defend his side of the radiologic question. There should be in this discussion a "radiumologist" and a radiologist, because, as Dr. Jesberg said and as the Jacksons' paper would indicate, we have not yet reached the point where we can speak definitely. I have great hopes for the effect of proper irradiation carried out by experts on cancer, because I have seen excellent results in the treatment of certain kinds of tumors of the larynx. I would say that the results depended on whether the tumor was radiosensitive or radioresistant. However, in association with Dr. Cutler in one of the largest institutions for the care of carcinoma of the larynx, namely the Veterans Administration Facility at Hines, Ill., I have seen similar results in the case of radioresistant tumors that were really operative and yet were subjected to irradiation at the patient's request. Recently Dr. Schall painted an excellent picture of laryngectomized patients and said truly that they are not a great unhappy family, as they are so often described. Most of the people who are cured of cancer of the larynx are glad that they are permitted to live on with an educated or artificial voice. If they become dependents now, since so many people are dependents they don't have to care so much about that. Most laryngectomized patients do become dependents, according to my experience. They are not productive, especially if they are salesmen. I am definitely at variance with Professor Coutard about making the fixed cord which is immovable from inflammation move again. I have not seen this happen. The inflammation is chronic and is not, according to radiologists, affected by irradiation. I do not think it should be considered in the prognosis. Dr. Jesberg also was definitely wrong when he said that for a tumor which was very sensitive to irradiation he would operate. I have seen the worst kind of results from such a procedure, namely rapid spread not only into the glands of the neck but throughout the system. The surgeon should be much more alert to the pathologist's decision as to what type tumor he is treating.

DR. CHEVALIER L. JACKSON, Philadelphia: I appreciated very much hearing Dr. Cutler's discussion. Dr. Jesberg and Dr. Beck have both spoken about lesions of the anterior commissure. We feel that it is much more important to consider the histologic picture with such lesions than with lesions in the middle third of the cord. It is with lesions of the anterior commissure that the final decision will depend on the histologic picture. The highly malignant lesion will certainly not be suitable for operation, but the lesion of low grade malignancy will be operable, and very successfully so, even if it does involve the anterior commissure. One of our tables lists thirty-four cases of lesions of the anterior commissure in which laryngofissure was done by the Chevalier Jackson anterior commissure technic. In this operation introduced by Dr. Chevalier Jackson in 1922, we divide the thyroid cartilage from the outside with a saw instead of clipping through the lesion with shears. Of our series of thirty-four patients, twenty-seven, or 79 per cent, were free from recurrence for three years. The last thing I wish to say is with regard to movement of the cord, a point which Dr. Beck mentioned. I have frequently seen irradiation restore the motion of a fixed cord whether the immovability was due to neoplastic infiltration or to inflammation.

**Muscle Physiology.**—Several observations by Bernard foreshadow the intensive work of the last decade in the field of muscle physiology. He found that blood leaving a contracted muscle is more venous than that leaving the same muscle at rest, i. e., although a living muscle always consumes oxygen, the consumption is increased during activity; and there is an accompanying increase in heat production. But if the motor nerve to the muscle is cut, there is very little oxygen consumed, even less than in a normal inactive muscle. This shows that, while the constant nerve impulses which keep the muscle in a state of semiactivity which we call *tonus* cause the muscle to consume a certain amount of oxygen, active contraction causes it to consume still more.—Olmsted, J. M. D.: Claude Bernard, Physiologist, New York, Harper & Bros., 1938.

## NEW STUDIES IN SURGICAL BACTERIOLOGY AND SURGICAL TECHNIC

WITH SPECIAL REFERENCE TO DISINFECTION  
OF THE SKIN

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BALTIMORE

Surgical technic has from the first suffered the lack of a quantitative test for degree of disinfection of the skin. It has been impossible to determine the precise effect of any hand disinfectant or stronger cutaneous germicide because the size of the bacterial flora could not be measured either before or after employment of the agent. In consequence there is a tremendous literature on the subject but little unanimity of opinion or uniformity in practice.

### A NEW QUANTITATIVE METHOD OF STUDYING THE BACTERIA OF THE SKIN

If a large number of basins of sterile water are prepared and the hands and forearms are scrubbed with soap and brush in a standard manner for exactly one minute in each basin, one after another, the washings will be found to contain a slowly diminishing number of bacteria. The cumulative totals plotted against time produce a curve. This is found to be a regular, logarithmic curve that is constant. From a study of this curve the size of the flora of the scrubbed area can be determined accurately.

Furthermore, by employing two such series of basins and plotting the two curves independently, the germicidal effect of any disinfectant used in the interval may be studied quantitatively. This introduces a new scale of germicidal value—the measured action of germicides in reducing the bacterial flora of skin as compared with the effect of scrubbing in a standard manner. The experiment shown in the accompanying table and chart will serve as an example to illustrate more fully application of the test.

The method also permits a much more accurate study of the bacterial flora of the skin than has been possible heretofore, lending itself admirably to investigation of the size and location of the bacterial flora as well as qualitative studies of the flora at various stages of degeneration, the mechanism of degeneration and reestablishment of the usual flora after degeneration.<sup>1</sup>

With generous help from colleagues and various groups of students, I have applied this new quantitative method to a reexamination of certain aspects of surgical bacteriology and surgical technic. The study has extended over a period of several years. Some of our results and conclusions are reported briefly herewith. A full description of the test and a more detailed account of the work on which the following conclusions are based will be published elsewhere.

### A SUMMARY OF RESULTS AND CONCLUSIONS

The bacterial flora of normal skin is found to be composed of "transients" and "residents."

Transients may be present in enormous numbers at times, but as a rule relatively few are present on grossly clean hands or on clean protected (unexposed) skin.

From the Department of Surgery, Chee-loo University, China, and the Department of Pathology and Bacteriology, Johns Hopkins University School of Medicine.

1. The word degeneration is used here in preference to disinfection to designate reduction in the total number of bacteria present, irrespective of whether the organisms are or are not pathogenic.

Transients, which are collected from extraneous sources, are comparatively easy to remove or kill. That is not true of the basic flora. Hence tests of germicidal power, which utilize test bacteria placed on skin and exposed subsequently to some disinfectant, may give thoroughly misleading results.

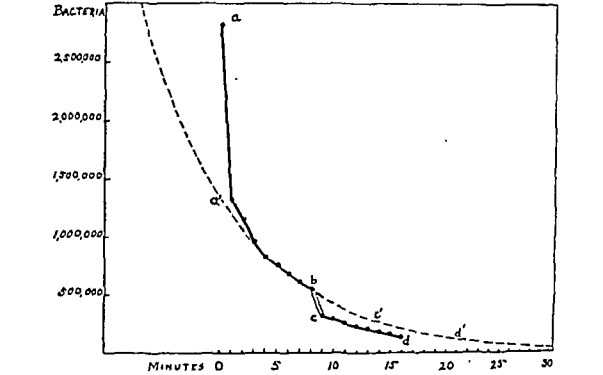
The size of the basic (or resident) flora at any given time is the net result of factors constantly acting, some to increase, others to lessen, the bacterial "population." Increase results largely from multiplication of resident organisms already present. Decrease is brought about by washing, friction of clothing and influences deleterious to bacterial life. Certain transients change their status and become residents, but this process seems to be a slow one and how it takes place is not clear. But the fact that it does happen makes it important to disinfect contaminated hands without undue delay.

The resident flora of my hands and arms, under conditions of ordinary life, tends to strike an equilibrium at about eight million micro-organisms.

This flora is located not in the skin nor to any extent in glands or hair follicles but on the skin.

The basic flora includes some pathogenic germs. If hands are in frequent contact with contaminated objects a dangerously large proportion of the resident bacteria may be pathogens. In such a case it is almost impossible to disinfect the hands. In this hitherto unsuspected manner a person may become a carrier of virulent organisms.

Ethyl alcohol has a very narrow range of effective germicidal concentrations. The optimum germicidal strength, both in vitro and on the skin, is 70 per cent by weight (not by volume as ordinarily prepared).<sup>2</sup> At precisely this concentration, alcohol is more effective than any other hand disinfectant now in general use. Each minute spent in this particular solution (at 25 C.) has a degerming effect equivalent to about six and one-



Bacteriologic effect of washing the hands and arms in 78.5 per cent (by weight) alcohol for one minute. The broken line *a'd'* represents the rate at which the basic flora of the author's hands and arms always are degermed by scrubbing in a standard manner. The solid line *ab* indicates the effect of scrubbing eight minutes, while *cd* shows the result of scrubbing seven minutes in the second series of basins. The initial deviation, *aa'*, from the broken line is due to contaminating (transient) bacteria purposely placed on the hands at the outset. So, of the initial number of 2,822,000 organisms, only 1,350,000 were "resident." This relatively small flora was due to the hands and arms having been well degermed two days previously and the usual flora not yet having been reestablished. The second deviation, *bc*, was due to use of the alcohol. It is clear that, by scrubbing 4.2 minutes, *bc'*, the same effect (as *bc*) could have been obtained. *cd* is equivalent to *c'd'*. Hence each minute spent in this particular solution of alcohol may be said to be equivalent to 4.2 minutes of scrubbing.

Results of an Experiment Done to Determine the Effect of Washing in 78.5 Per Cent (by Weight) Alcohol on the Bacterial Flora of Hands and Arms

Basin	Scrubbing Time, Minutes	Total Bacterial Count for Basin, Organisms	Cumulative Totals Washed Off, Organisms	Actual Totals or Size of Flora Left, Organisms
				2,822,370 (a)
1	1	1,497,440	2,272,370	1,324,930
2	1	166,320	774,930	1,158,610
3	1	197,960	608,610	960,650
4	1	132,770	410,650	827,880
5	1	66,300	277,880	761,580
6	1	74,000	211,580	687,580
7	1	74,680	137,580	612,720
8	1	62,720	62,720	550,000 (b)
At this point hands and arms dried in the air and then washed without friction in 78.5 per cent (by weight) alcohol for exactly sixty seconds. Scrubbing resumed immediately. Temperature of alcohol 25 C.				
				318,595 (c)
9	1	30,070	178,595	288,525
10	1	31,840	148,525	256,685
11	1	22,655	116,685	234,030
12	1	28,420	94,030	205,610
13	1	24,360	69,610	181,250
14	1	17,730	41,250	163,520
15	1	23,520	23,520	140,000 (d)

(a) Total number of bacteria on the hands and arms at the beginning of the experiment; (b) after eight minutes of scrubbing; (c) after application of the germicide; (d) after the second period of scrubbing; b and d are arrived at by mathematical projection of the curves produced.

Scrubbing with brush, soap and warm water, as practiced by me, reduces this basic flora at a constant rate. Irrespective of the initial size of the flora, the number of bacteria is reduced by approximately one half with each six minutes of scrubbing. The kind of soap used makes no difference. Variations in the temperature of the water do not influence the rate appreciably. The amount of vigor used in brushing is a very important factor, however. Sterile water has been found to possess no advantage over ordinary tap water in reducing this flora.

half minutes of scrubbing. This effect may be increased considerably by friction, i. e. by rubbing with gauze or a rough wash cloth. Even slight variations from that particular concentration of alcohol results in marked decrease of bactericidal power. Sixty per cent by weight (about 70 per cent by volume) is almost worthless.

Mercury bichloride solutions do not reduce the flora on the skin appreciably. Paradoxically, a sterile cutaneous surface may be produced. This phenomenon is due, we believe, to the formation of a transparent "film" on the skin under which the bacteria are imprisoned. There conditions are so suitable to life that multiplication takes place, the existing bacterial flora doubling every fifty minutes. The "film" may be broken up, either with an alkaline sulfide or by prolonged friction, whereupon the bacteria are released uninjured.

The same phenomenon is observed when potassium mercuric iodide (biniodide) or Harrington's solution is used. Neither of these is a true germicide when applied to the skin. When tested, these agents should always be followed by an alkaline sulfide.

Kelly's method of hand disinfection (with hot saturated solutions of potassium permanganate and oxalic acid) is very effective. The procedure requires from two and one-half to more than five minutes, depending

2. It is important to differentiate clearly in solutions of alcohol between per cent by volume and per cent by weight. Per cent by weight solutions are exact and invariable. Per cent by volume solutions, as ordinarily prepared, are inexact and undependable owing to three uncontrolled variables—temperature expansion, specific gravity and reaction concentration. Thus 70 per cent alcohol by weight (always the same) is the equivalent of 76.8 per cent by volume if the latter is prepared at 15 C. but is the equivalent of 80.5 per cent by volume if the volumetric measurement is made at 25 C. Accurate weight per cent solutions can be prepared from commercial (95 per cent) alcohol with the help of hydrometer, thermometer and appropriate tables. The following formula will give a solution approximately 70 per cent by weight: 95 per cent alcohol at 25 C. 815 cc., plus cold distilled water sufficient to make 1,000 cc.

on the temperature of the solutions. The total degerming effects are equivalent to between twenty and thirty minutes of scrubbing.

The lime and soda method is also very effective. When rubbing with the paste was continued for four minutes the reduction of flora was as great as could be accomplished by twenty minutes of scrubbing.

Saponated solution of cresol, though a relatively strong germicide against test organisms *in vitro* (a claim which we have verified), proved worthless as a disinfectant of the skin; 1:400 and 1:200 solutions, used without friction at 25 C., do not reduce the flora appreciably. In 1:100 solution, which causes some burning and anesthesia of skin, the flora is reduced about as rapidly (or as slowly) as scrubbing.

A search for a more nearly ideal hand disinfectant has resulted in the production of a new germicidal mixture which seems to possess certain advantages over any of the agents now in general use. It is powerfully germicidal, each minute spent in it (at 25 C., without friction) being equivalent to more than eleven minutes of scrubbing. It is simple and pleasant to use. It does not irritate or injure the skin. It is more stable than simple ethyl alcohol solutions. This germicide consists of ethyl alcohol 50 parts by weight, normal propyl alcohol 20 parts by weight and water 30 parts by weight. It may be prepared as follows: ethyl alcohol (95 per cent) 675 cc., pure n-propyl alcohol 250 cc., distilled water 250 cc., all measurements being made at 25 C.

By rational and conscientious use of the most effective means, the bacterial flora of the hands can be reduced to a relatively low figure but practically never to zero. The remaining organisms may, and on surgeons' hands often do, include pathogens. Hence the necessity for wearing gloves when operating.

Beneath rubber gloves, however, the bacteria remaining on the skin multiply rapidly, their number doubling every forty minutes if the hands are dry or every fifty minutes if the gloves have been put on wet. If gloves are worn long enough, the cutaneous flora may increase until it exceeds by far the ordinary flora. I found that on one occasion the bacterial count of my hands and arms had increased to more than 31,000,000. If pathogens are present they participate proportionately in this multiplication. No means has yet been found to prevent or delay this increase. These extraordinary bacterial "populations," we find, cannot be reduced any more rapidly than the ordinary. This phenomenon of rapid increase of cutaneous flora does not occur under cotton gloves or ordinary clothing.

The basic flora of protected skin per unit area is no smaller than that of the hands.

Ether, a representative of a group of the stronger germicides thought to disinfect skin chiefly by means of detergent properties, when subjected to our quantitative test proved utterly powerless to reduce the basic flora of clean skin.

Freshly prepared U. S. P. tincture of iodine (7 per cent), applied to grease-free skin and followed by an antidote, came nearer to full sterilization of the epidermis than any other germicide tested. U. S. P. "half-strength" tincture of iodine (3.5 per cent) proved far less effective, reducing the flora irregularly, but on the average by less than half. Two per cent iodine in 70 per cent (by weight) alcohol was much more effective, lowering the bacterial count to nearly 18 per cent of its original size. On drying, the germicidal action of iodine

practically ceases. The 2 per cent iodine in 70 per cent alcohol solution has certain important advantages: even spread, slow evaporation, nonirritation, and contributory bactericidal effect of the 70 per cent alcohol.

Mercurochrome, a prominent representative of a large group of the newer germicides, the organic compounds of mercury or silver, was tested. From bacteriostatic and bacteriocidal standpoints, mercurochrome was found to be similar in many respects to the inorganic salts of mercury. If no antidote is used, an exaggerated idea of its germicidal power is obtained. Aqueous solutions of mercurochrome on the skin may produce a nearly germ-free surface, but subsequent use of 10 per cent ammonium sulfide will show that the bacterial flora has been reduced little if any. Scott's alcohol-acetone-2 per cent solution of mercurochrome, applied liberally and allowed to dry slowly, reduced the bacteria of the skin to about one-third their original number. This whole group of germicides, the organic compounds of heavy metals, needs to be reinvestigated, appropriate antidotes being used.

After the skin has been degermed, reestablishment of the usual flora proceeds slowly (except under rubber gloves), apparently at a rate represented by a sigmoid curve. When the hands and arms have been thoroughly "disinfected," the number of bacteria being reduced, say, to 200,000, full reestablishment of the ordinary flora may be expected in about a week.

Parallel studies of our quantitative test on the one hand and the commonly used scraping and rubbing tests for cutaneous contamination on the other show that both of those time-honored methods become increasingly untrustworthy as the flora of the skin diminishes.

#### PRACTICAL RECOMMENDATIONS

The following principles and procedures are based on our experimental studies. Before recommending them, however, we subjected them critically to a prolonged test of clinical application, with highly satisfactory results.

*Preoperative Preparation of Hands.*—1. The hands are scrubbed with soap, a good brush and warm water for at least seven minutes. This will usually suffice to remove gross dirt, transient bacteria and fats, and incidentally about half the basic flora. The nails should be short and clean at the start.

2. The resident flora is much more effectively attacked by germicides than by scrubbing. We recommend ethyl alcohol, 70 per cent by weight, or the mixture of alcohols described. These solutions should be freshly and accurately prepared. Before entering the alcohol basin, the hands and arms should be dried thoroughly with a sterile towel, for to carry water into the alcohol will weaken the solution and markedly lessen its germicidal power. In the alcohol basin the skin should be rubbed firmly with sterile gauze or a washcloth.

The time spent in these solutions is of the utmost importance. We suggest that ethyl alcohol be used with friction for three minutes by the clock or the mixture of alcohols for two. This may be expected to reduce the original flora from 50 per cent (result of scrubbing) to something less than 2 per cent.

The occasional operator will increase the margin of safety by washing also in a 1:1,000 bichloride or 1:500 biniodide solution for one minute. The mercuric salt should follow, never precede, the alcohol, for the film formed by the mercurial is impervious to alcohol as well

as to bacteria. Bichloride, biniodide and Harrington's solutions are not recommended, however, for hands that must be disinfected frequently.

3. Gloves and gown are put on. An ungloved hand inevitably increases the risk of wound infection. In operating rooms where expense is not a major consideration, where only perfect (unpatched) gloves are used and where preparation of gloves are in highly competent hands, we have shown dry gloves to be preferable, and even safer. Elsewhere wet gloves will probably have a larger margin of safety. In lieu of gloves, the operator should wash his hands in bichloride or biniodide of mercury.

4. Between operations the hands should be washed in a germicidal solution in order to counteract the increase of cutaneous bacteria which has taken place beneath the gloves. A useful rule is one minute in alcohol for every hour that the gloves have been worn.

*Preparation of the Field of Operation.*—Preparation of the patient's skin the day before operation by wrapping the part in sterile towels is psychologically harmful and bacteriologically useless. Before coming to the operating room the patient should receive a bath, however, the site of operation being especially well washed with soap and water to remove dirt, most of the fats and any transient bacteria. If, as in the presence of a wound, this is not possible, a chemical detergent should be used.

Immediately before operation the site of incision should be washed with gauze and 70 per cent (by weight) alcohol or the suggested mixture of alcohols. It should be allowed to dry slowly, for in disinfection time is a factor that cannot be ignored.

This is to be followed by one of the stronger germicides. U. S. P. tincture of iodine (7 per cent) is extremely effective but in many cases too strong a solution to be tolerated or used safely. We recommend weaker solutions of iodine dissolved in 70 per cent (by weight) alcohol. After application, iodine solutions should be permitted to dry slowly. Washing a dried coat of iodine off the skin with alcohol increases rather than diminishes the total germicidal effect.

As an alternative to the iodine technic, the field of operation may be painted with Scott's alcohol-acetone-2 per cent solution of mercurochrome, or an irregular area such as that of the hand or foot may be soaked for a minute in 1:500 biniodide solution. In either case an aseptic surface will be produced. But the line of incision must first be specially prepared (disinfected), else the knife will necessarily pass through germ-laden skin beneath the "film." One way to do this is to rub the site of incision for two or three minutes firmly with gauze and 70 per cent (by weight) alcohol or our mixture of alcohols.

*Disinfection of Contaminated Hands.*—Ordinary hands, contaminated by contact with infectious patients or materials, are not difficult to disinfect. Saponated solution of cresol, however, is almost useless for the purpose, and solutions of bichloride or biniodide of mercury may be actually dangerous. We recommend the following as a simple dependable method for routine use:

1. The hands should be washed as soon as possible with soap and running water for at least thirty seconds. This may be expected to remove about nine tenths of the contaminating organisms. If there is pus, blood,

secretion from the wound, saliva, mucus or other infectious material on the hands, washing should be continued for a minute or more, perhaps with the use of a brush.

2. The hands should be well dried on an individual towel.

3. Every part of the hands should be wet with 70 per cent (by weight) alcohol. A few cubic centimeters dripped on the hands will suffice. The alcohol should not be wiped or shaken off but the skin should be allowed to dry by evaporation. It is the germicidal action that is required, and that takes time.

909 University Parkway.

## PHOTOGRAPHY OF THE UTERINE CERVIX

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The present knowledge of medicine must be handed on to students, and teaching can be accomplished more advantageously with a combination of auditory and visual methods than by either method alone. Photographs are also of value to the practitioner as office records. The physician may wish to know what the exact appearance of the cervix, or any other lesion, was six months previously.

The patient also appreciates knowing why the cervix or other inaccessible part of the body needs repair or other treatment. She has no idea of the appearance of the cervix because she has never seen it and has never been aware of any sensation from it, since there are no sensory nerve endings in it. No other part of the body undergoes as much injury or is so neglected after being injured. The cervix is also the sharp junction of two distinctly different types of epithelium, which means that it is constantly subject to change due to the erosion and healing processes going on in such an area. Other parts of the body may lend themselves just as readily as the cervix to photographic records. Portrayal of operative procedures and photographs of pathologic tissue in situ are both valuable and should be preserved not only for records but for use in teaching.

In the field of gynecology and obstetrics, teaching material is somewhat more difficult to find than in other branches of medicine; therefore, every effort possible must be made to record by accurate drawings and photographs examples of pathologic lesions and normal tissue.

Not only must this material be recorded, but it must be done in such a way that it is easily available for teaching purposes. The records must be where they can be readily shown and they must be shown repeatedly.

Students spend long hours in clinics attempting to see examples of lesions about which they have read, but most find by the time their course is over that there are many important lesions which they have not had an opportunity to see. By making accurate colored photographs over a period of years of the many differ-

Read before the Section on Obstetrics and Gynecology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.

ent cases, one can supplement the reading course by actual photographs in color.

With these points in mind, I have for the past several years been attempting to devise a means whereby good photographs could be made with the least possible expenditure of time and with the least discomfort to the patient. The various devices assembled here are by no means perfect, but this paper is published with the hope that others interested will contribute valuable suggestions.

Many difficulties were encountered in an attempt to photograph as small an object as the cervix at close range. The usual tripod was found to be too cumbersome; a single shaft on a heavy round metal base has proved much easier to handle. It can be placed close

Another difficulty was the distance from object to camera, and this was overcome most readily by using a Speed-o-Copy attachment with three extension tubes and a 90 mm. f/4.5 telephoto lens. With the use of this attachment, extension tubes and telephoto lens, the image on the colored film is approximately life size and the end of the lens is kept 18 cm. from the cervix. This distance allows the lens to escape touching the speculum. The Speed-o-Copy attachment has a ground glass for focusing, and over this is a detachable magnifying lens which makes possible a very accurate focus. When the cervix is in sharp focus the ground glass and lens swing up, the camera lifts up into the position formerly held by the ground glass, and it is locked there while the exposure is made (figs. 1 and 2).

A third difficulty was proper illumination of the cervix. Various speculums with lights built inside were tried, but none were bright enough and most of them caused discomfort. Two "Good-Lites" are now used, one on either side of the lens, and they are fastened to the base of the Speed-o-Copy attachment by small universal joints. These lights are commonly used by otolaryngologists on a headband. The rheostats for the lights are attached to the standard and help to lend weight.

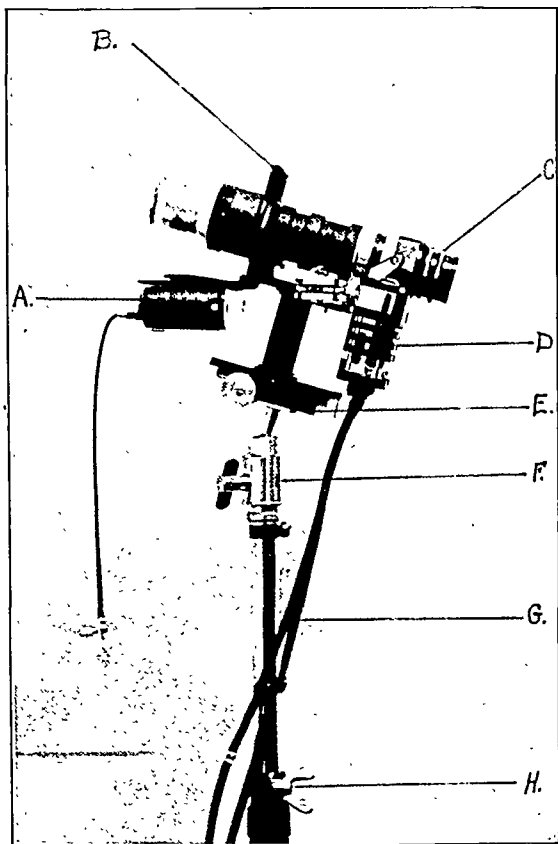


Fig. 1.—Camera in position for focusing. A, Leica camera; B, Speed-o-Copy (D. Paul Shull, manufacturer, Los Angeles) with three extension tubes; C, 90 mm. f/4.5 lens; D, two "Good-Lites"; E, microscope stage attached above to base of Speed-o-Copy and below to F, Leica universal ball joint; G, rheostat cords; H, expansion screw allowing inner rod to be raised and lowered.

to the examining table and moved easily forward or backward to the approximate focal distance. This rod is so constructed as to allow the camera to be either raised or lowered. A small candid camera lends itself to quick work, but any other camera may be used. Up to the present time, the best colored film is available only in 35 mm. size, and since it gives a very accurate colored picture the small candid camera seemed best to start with. The camera is not permanently attached to the assembly of the various devices but may be used as a candid camera merely by unscrewing it from the Speed-o-Copy attachment and replacing the usual lens. In other words, the use of the camera is not restricted to the office or clinic but is available for other purposes.

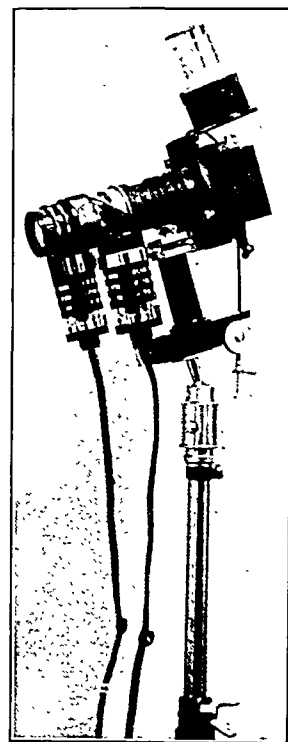


Fig. 2.—Camera in position for making picture.

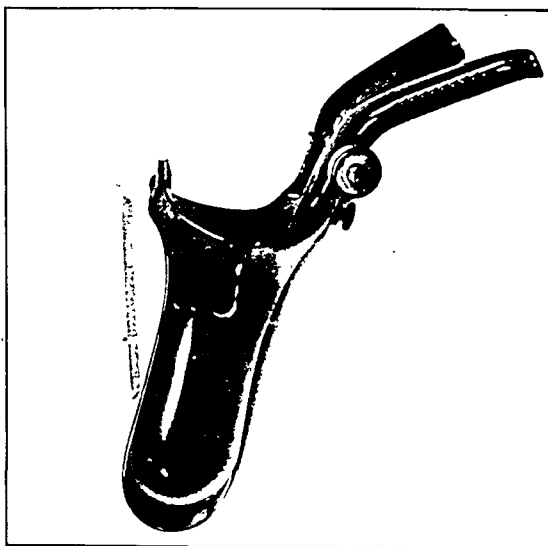


Fig. 3.—Bivalve black nickel vaginal speculum and piece of thin rubber Penrose tube.

Another problem was to obtain an accurate focus. In order to get this quickly the whole outfit was attached by a rigid tubular post to a microscope stage.



By turning the screw of this stage, one moves the camera and all its attachments forward or backward in the same plane. The entire assembly is attached to the standard by a large ball universal joint which allows it to be pointed in any direction the vaginal canal may assume. Once the mechanism is placed at the proper height and directed properly, the microscope stage permits a quick accurate focus.

Getting proper exposure of the cervix and an aperture through which a photograph could be taken was another perplexity. The comfort of the patient is of great importance and must be considered, for she must wait until the camera is adjusted properly. A large-sized bivalve speculum was found to be the most comfortable and still permit an aperture large enough; made of black nickel, it gives very little reflection. In order to hold the lateral vaginal walls back, a piece of large-sized Penrose rubber drain may be pulled on to the speculum before it is inserted. As the blades are spread apart, the tension caused by stretching the rubber keeps the vaginal walls perpendicular (figs. 3, 4 and 5).

Kodachrome film is used and the films are mounted as lantern slides. The slides,  $3\frac{1}{4}$  by  $4\frac{1}{4}$  inches (8.2 by 10.8 cm.), are made for regular stereopticons because much more light is available in them; however, the small slide, 1 by  $1\frac{1}{2}$  inches (2.5 by 3.8 cm.), may be used. Kodachrome film has no grain in it and with a 1,000 watt lamp and a  $6\frac{1}{2}$  inch (16.5 cm.) lens on a projector, a small 35 mm. picture can be made approximately 10 feet square at 40 feet with no loss of fine detail.

Black and white film can also be used, and from these negatives enlargements are made. In order to increase the depth of focus, the lens is closed to f/9 or smaller, and it has been found that an exposure of four

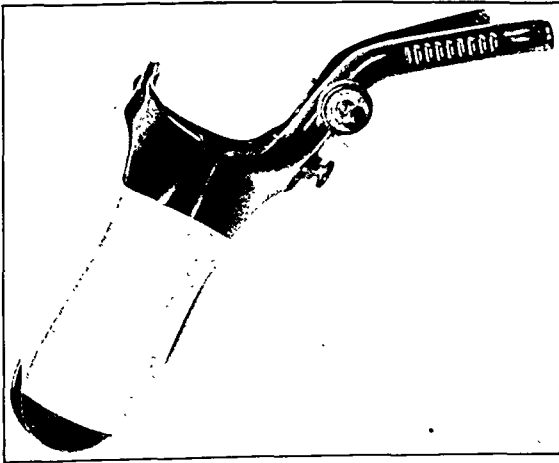


Fig. 4.—Rubber tubing drawn over blades of speculum and ready for insertion.

fifths of a second at f/9 has been satisfactory in most of our work. One light may be a little less bright, thus overcoming some of the difficulty in photographing a spherical object. This, however, is not necessary when Kodachrome film is used, since the color itself gives the impression of depth in the photograph. Photographs can be made in from five to ten minutes with the use of this mechanism and, as every one knows, the saving of time is desirable during a busy office or clinic period.

This assembly has not been patented and will not be; however, the various parts of which it is composed are patented articles. The mechanism is being assembled by the General Scientific Instrument Company of Chicago, and I do not and will not receive any remuneration from it. It is only hoped that others will be stimulated to make good photographs, not of the cervix alone but of lesions in other organs, and will report their work at some future date.

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#### ABSTRACT OF DISCUSSION

DR. J. M. BRUNER, Des Moines, Iowa: I should like to express my appreciation of Dr. Galloway's paper. Heretofore lesions of the cervix have been illustrated by drawings, which

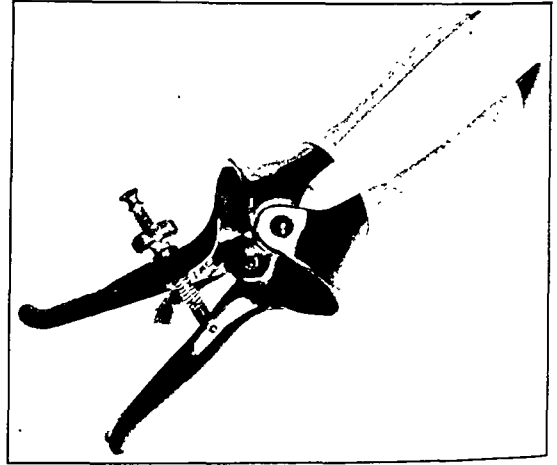


Fig. 5.—As the speculum blades are separated the tension caused by stretching the rubber keeps the lateral vaginal walls perpendicular.

were often inaccurate. It is surprising that no good photographs of the cervix are to be found in textbooks. Years ago my attention was called to this fact by an article by Mr. Ralph P. Creer of Chicago (*Photography of the Cervix Uteri, Journal of the Biological Photographic Association*, December 1935). At the time I was conducting one of the gynecology clinics of the Broadlawns County Hospital at Des Moines, Iowa. Many interesting lesions of the cervix were being seen, and it seemed desirable to make a photographic record of these lesions before and after treatment. For this purpose I designed a special tubular speculum which provides unexcelled exposure of the cervix for photography. The lights are placed within the speculum on one side only, in order to produce the maximum degree of modeling in the cervix. The camera used is a Leica with sliding ground-glass attachment. The technique for this work was published in an article by Dr. L. E. Rosebrook and myself in the *Journal of the Biological Photographic Association*, September 1936, and in the *American Journal of Obstetrics and Gynecology*, December 1937. Color photographs of the cervix make beautiful lantern slides. Such photographs, however, cannot be reproduced for publication. For this purpose black and white negatives are essential. Good black and white negatives are much more difficult to obtain because they lack the third dimensional properties of color film. They do, however, make excellent illustrations for textbooks and scientific articles.

**No Life Without Proteins.**—Proteins represent the stream of life. They make up the vital part of that essential jelly material of the living cell—the protoplasm. The beginning of life on this and perhaps a few other fortunate planets must have been associated with the formation of proteins. This word means "to take first place," for there is no life without proteins. The name was the lucky choice of Mulder, one of the first investigators.—Furnas, C. C., and Furnas, S. M.: *Man, Bread and Destiny*, New York, Reynal & Hitchcock, 1937.

REOPENING LIGATED TUBES BY  
UTERINE INSUFFLATION WITH  
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NEW YORK

Surgical sterilization by tubal ligation has a disquieting effect on some patients, leaving them unreconciled to the artificially induced sterility. Certain circumstances besides remorse and psychic depression occasionally arise after surgical sterilization which make the retrieval of the forfeited fertility eminently desirable. Such is the loss of an only child or more rarely the loss of two or three children or marriage to a second husband with whom children are keenly desired. The loss of fertility is particularly felt by women whose health is unexpectedly improved or wholly restored.

To remove the obstacle to conception, another laparotomy must be considered. But since this involves the risk of a surgical operation, postoperative convalescence and possibly also an economic burden, it is not particularly agreeable to the patient nor is it readily assented to by the husband.

For such women any method that might accomplish the reopening of the tubes without necessarily resorting to a laparotomy would appear to meet a real need. In uterotubal insufflation a nonoperative method has been found which offers this possibility. Its application for this purpose is supported by a number of successful therapeutic results following uterotubal insufflation in cases of involuntary sterility due to strictures of the fallopian tubes and peritubal adhesions. In these cases pregnancy has occurred within one or several months after treatment. The pressure to which the carbon dioxide is raised in these strictured tubes often reaches

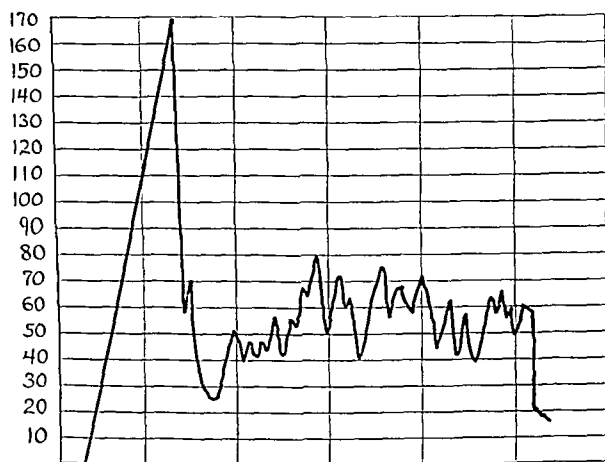


Chart 1.—Tubal insufflation Oct. 1, 1931. Initial rise of pressure to 170 mm. of mercury; sharp drop at point where the obstruction was relieved to 60 mm. and 25 mm., after which strong tubal contraction waves were recorded typical of normally patent fallopian tubes.

200 mm. of mercury before patency is established. By widening the opening in the tubal lumen, the impediment to conception is removed.

An accidental observation made in 1931 on a patient who had been sterilized by tubal ligation gave the clue to the possible therapeutic use of carbon dioxide insufflation after ligation of the tubes. D. S. had an only child who had been delivered by cesarean section, at which time the fallopian tubes were tied and cut and

the severed lumens were peritonealized. Contemplating remarriage, she wanted to know whether she could possibly conceive again. During tubal insufflation the pressure rose to 170 mm. of mercury and suddenly dropped to 60 mm., after which rhythmic contractions and relaxations were recorded on the kymograph drum (chart 1). There were typical shoulder pains, and a subphrenic pneumoperitoneum was demonstrable fluoroscopically. She became pregnant two years after this examination. Several years later a uterine insufflation showed the tubes to be open within normal limits and functioning (chart 2).

I did not have occasion to reopen ligated tubes by this method until 1937, when this question arose in connection with a study of the Head zones and distri-

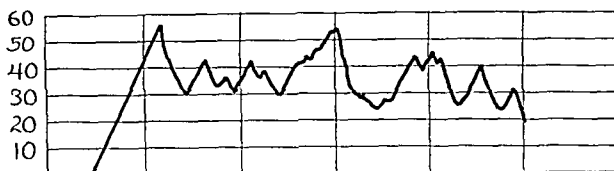


Chart 2.—Tubal insufflation in same patient Oct. 11, 1937, showing tubal patency at normal pressure levels.

bution of pain coincident to tubal distention which was produced by uterine insufflation with carbon dioxide.<sup>1</sup> The study was made in young women who had recently been sterilized by tubal ligation. The ligatures had been intentionally placed at different portions of the fallopian tubes. It was found that when the pressure exceeded 120 mm. of mercury there was a sudden sharp drop, indicating that the tube or tubes yielded at the ligated points. The carbon dioxide passed into the peritoneal cavity and the tubes exhibited rhythmic contractions. Since the sterilization was indicated on medical grounds, these patients were duly instructed in contraception.

Based on five similar experiences, it seems justifiable to say that one or several of the women whose tubes were reopened could become pregnant again if they chose to. This possibility obviously puts a different psychologic aspect on tubal ligation in the case of women who hope for a return of reproductive function. The assurance of retrievability enabled three patients during the past year to go through the operation with an untroubled mind.

As to the manner in which insufflation opens up ligated tubes, it has been noted that whether the tubes are previously crushed, as in the Madlener operation, or not crushed, as in the Pomeroy method, the operations which are preferred by most surgeons, the pathologic change induced is localized at the point of ligation. Observations on the local condition following the operation are fairly uniform. A small fibrous band connects the severed end of the tubal loop, or fine adhesions bind them to adjacent viscera.<sup>2</sup> The stricture, though complete, is limited to a very thin segment of the endosalpinx and tubal serosa in contrast to pathologic strictures, which as a rule occupy more extensive portions of the lumen of the tube.

As fallopian tubes that have been ligated were normal previous to the sterilizing operation, they remain normal except at the point of ligation. This renders the surgical stricture vulnerable to intratubal pressure.

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When it becomes desirable to reestablish tubal patency after the Madlener or Pomeroy operation, the same technic of uterotubal insufflation can be adopted as in testing for tubal patency in cases of involuntary sterility. When I originally suggested this method to test the security of tubal ligation, I did not realize that higher pressures than those required for normal patency might overcome the artificially induced obstruction. Later experience has shown that this is possible. In this connection it is not altogether strange that pregnancy should follow the opening of otherwise normal tubes which have been ligated and severed at different points for purposes of sterilization, since pregnancy has been known to occur in cases in which diseased tubes were resected at practically any point of their entire length, including the uterine insertion.

Patency was reestablished in five cases following tubal ligation by pressures below 160 mm. of mercury. The operation of ligation had been performed by different gynecologists. Apparently the more recent the ligation the less pressure is required to open up the tubes. Unless the interstitial portion of the tube has been resected, the artificially induced obstruction should yield to insufflation at a pressure of 200 mm. of mercury or less. In experienced hands the pressure level may be increased to 250 mm. of mercury. The latter, however, is recommended only as a therapeutic measure for the specific purpose of effecting a reopening of ligated tubes. If the insufflation fails on the first trial to open the tubes, it can be conveniently repeated at suitable intervals. Should pregnancy not soon take place though tubal patency has been restored, the patient has the reassurance that the mechanical closure is no longer responsible for the sterility.

The question naturally arises whether fluid mediums may not be used instead of carbon dioxide to reopen ligated tubes. If iodized poppyseed oil or other iodized oils are considered there are several disadvantages: 1. Retention of oil at or near the tight opening may induce foreign body reaction and organic obliteration.<sup>3</sup> 2. The pressure control is not as accurate as when carbon dioxide is used. 3. The injection of iodized oils cannot be repeated as conveniently and safely as insufflation with carbon dioxide. The latter has the great advantage of being used under a constant rate of flow, regulated by a reduction valve, the gas being promptly resorbed and leaving no residue.

If one prefers to employ fluids it is advisable to use skiodan, hippuran or any of the quickly resorbable crystalloids of iodine, which can be injected with the aid of the kymographic insufflation apparatus. I have not used these radiopaque mediums for this purpose because the data with regard to the points of ligation, the only point to be adduced by opaque mediums, were already available. If such data should not be at hand, one could locate the obstructions by the insufflation method.<sup>4</sup>

As to the technic, it is only necessary to mention that the flow of carbon dioxide is regulated at the rate of 1 cc. per second or slower, the pressure rise and pain reaction being observed if any are present. About 100 cc. of gas is adequate and the procedure requires from two to three minutes at the first trial.

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## TETRALOGY OF FALLOT

REPORT OF A CASE IN A MAN WHO LIVED  
TO HIS FORTY-FIRST YEAR

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AND

NATHAN FLAXMAN, M.D.

CHICAGO

A major congenital anomaly of the heart associated with the development of the bulbus cordis<sup>1</sup> is the unusual and rare condition first noted by Peacock<sup>2</sup> and later fully described by Fallot.<sup>3</sup> The tetralogy of Fallot consists of the combination of an interventricular septal defect, pulmonary stenosis and insufficiency, dextroposition of the aorta and hypertrophy of the right ventricle. Abbott<sup>4</sup> ascribed this combination of lesions, largely on the basis of studies by Keith, to an arrest of development before the eighth week of embryonic life. She<sup>5</sup> cited seventy-three cases of the tetralogy in her comprehensive summary of the literature in 1928. The oldest patient in her series was 36 years of age and the average age in the series was 11 years.

The outstanding case of this type in the literature is the report by White and Sprague<sup>6</sup> of a noted musician who lived to his sixtieth year, surpassing in age all patients previously reported by more than twenty-three years. Leadingham<sup>7</sup> reported the case of a white girl aged 15 years who had been short of breath and cyanotic all her life; the cause of death was a subacute bacterial endocarditis of the pulmonary valve which had caused occlusion of the narrow pulmonary orifice. Blackford<sup>8</sup> related a clinical case in a Negro youth aged 20 who had always been short of breath, had clubbed fingers, and had the usual polycythemia. White and Boyes<sup>9</sup> cited the case in a white woman aged 21 with the tetralogy but whose death was due to a subacute bacterial endocarditis of the tricuspid valve and the pulmonary artery. Segall's<sup>10</sup> case of a white man aged 23 had been discussed by Abbott<sup>5</sup> in her review. Two other cases were reported in infants;<sup>11</sup> in one there was also a redundant left ductus arteriosus and in the other an anomalous band in the right auricle.

A much rarer congenital anomaly of the heart similar to this tetralogy is the Eisenmenger<sup>12</sup> type, described

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4. Rubin, I. C.: Tubal Strictures and Their Localization by Means of Uterotubal Insufflation and the Kymograph with Notes on the Comparative Value of Lipiodol, *Am. J. Obst. & Gynec.* 20:28 (July) 1930.

by him in 1897, which presents no pulmonary stenosis but a thick, wide pulmonary conus, so that a pulmonary insufficiency without obstruction is present. Baumgartner and Abbott<sup>13</sup> reported a case of this type in a white man aged 20 presenting impaired conduction and paralysis of the recurrent laryngeal nerve from pressure of the hypertrophied pulmonary conus; the patient died of a cerebral abscess. Rosedale<sup>14</sup> reported a third case of the Eisenmenger type in a white boy aged 10 years. Talley and Fowler<sup>15</sup> reported the fourth case of this kind in a white woman aged 31 who had had a normal physical and mental development, had passed through two pregnancies and had been able to take care of her house until a month before her death.

The case of the tetralogy of Fallot that we report is the first in which a clinical diagnosis was established (I. F. V.) and confirmed at postmortem examination

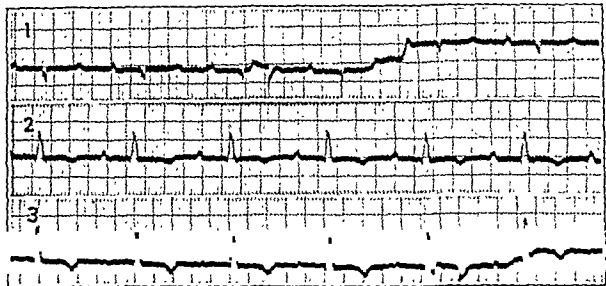


Fig. 1.—Electrocardiographic tracing in tetralogy of Fallot. Note prolonged PR conduction, right axis deviation, gross distortion of ventricular complexes and prolonged ST interval.

in the Cook County Hospital. The rarity of congenital heart disease at such a large institution may well be emphasized, as only ninety-nine cases (1 per cent) have been noted in 9,500 autopsy protocols in the period from 1929 to 1938. This incidence of congenital heart disease may be compared with and is as common at the Massachusetts General Hospital,<sup>16</sup> where sixty-seven cases (0.9 per cent) were noted in 7,500 postmortem examinations, and at the Johns Hopkins Hospital,<sup>17</sup> where 170 cases (1.29 per cent) were noted in 13,115 autopsies. Our case is also of unusual interest because the patient lived to the age of 41 years, five years longer than in any case reported previously with the exception of that of the noted musician,<sup>6</sup> and the cause of death was not in any way connected with the multiple cardiac abnormalities.

#### REPORT OF CASE

A man aged 41, a laborer, fairly well developed, was admitted to the medical service of the Cook County Hospital June 4, 1936, complaining of shortness of breath of thirty-five years' duration and swelling of the legs on and off during the past five years. He had had "heart trouble" as long as he could remember. Except for the shortness of breath he had been fairly well until 1931, when his legs became swollen. The swelling persisted a few weeks and then disappeared, only to return again. He had been attending the cardiac clinic of a medical

dispensary very irregularly for the previous five years. The day before admission to the hospital he had a "fainting spell" and fell, injuring the right circumorbital region.

Marked cyanosis and clubbed fingers were evident. A diffuse apex impulse was visible in the sixth left intercostal space at the midaxillary line. There was a palpable systolic thrill over the entire precordial area. The right border of the heart was 6 cm. to the right of the midsternal line, and the left border was in the midaxillary line. The systolic blood pressure was 168, the diastolic 100, the pulse rate 56. There was a long, very loud systolic murmur audible over the entire precordial area and over the cardiac area well to the right of the sternum. This long murmur was propagated upward into the vessels of the neck. There was a long diastolic murmur with the punctum maximum at the third left intercostal space at the margin of the sternum. The systolic murmur over the aortic and pulmonic areas was much louder than the diastolic murmur. The liver edge was palpable below the right costal margin. There was brown pigmentation, thickening with lichenification, and scaling of the skin on the lower half of the legs.

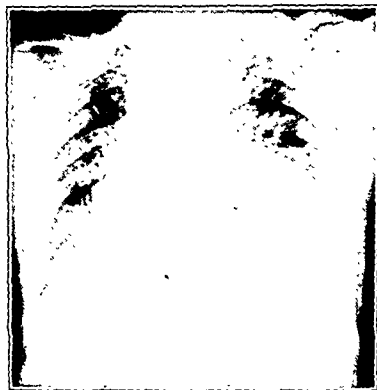


Fig. 2.—Heart shadow occupies most of the lower part of the chest. The wide vessel shadow at the base is due to the widely dilated first portion of the aorta.



Fig. 3.—Anterior view of the heart with the left ventricle open. Arrow-head points to basal interventricular septum defect.

13. Baumgartner, E. A., and Abbott, Maude E.: Intraventricular Septal Defect with Dextroposition of the Aorta and Dilatation of the Pulmonary Artery ("Eisenmenger Complex") Terminating by Cerebral Abscess, *Am. J. M. Sc.* 177: 639 (May) 1929.

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An electrocardiogram taken June 8 revealed an unusual picture (fig. 1). The rate was 60 and regular. Right axis deviation was noted. The P waves were prominent in all leads but diphasic in lead 3. The PR interval was prolonged to 0.28 second. The QRS complex was 0.08 second and grossly notched. The ST interval, while isoelectric, was prolonged, measuring 0.28 second. The T waves were inverted



Fig. 4.—Anterior view with open right ventricle. Aorta and pulmonary artery arise from the right ventricle. The interseptum defect is indicated by the tails of the arrow, with the arrowhead in the rightsided aorta. Vertical glass rod extends from the right ventricle into the stenosed pulmonary artery.

in leads 2 and 3. This abnormal type of electrocardiogram was interpreted as being related, probably, to the anatomic variations in the bundle of His and its branches, induced by the basal interventricular septal defect. Impulse transmission must have necessarily taken an abnormal course over the conduction system because of the distortion of the conducting mechanism. The prolonged PR interval, however, may have been the result of the uremic syndrome.

Fluoroscopy of the chest revealed considerable enlargement of the right border of the heart with marked enlargement also to the left and upward. The pulmonary conus was not visualized. Barium sulfate by mouth showed a diminished retrocardiac space but no compression of the esophagus. A 2 meter chest plate revealed enormous cardiac enlargement (fig. 2).

Chemical analysis of the blood taken on the same day revealed a urea nitrogen content of 130 and a creatinine content of 11 mg. per hundred cubic centimeters. The patient's condition changed at 2 p. m. June 9, when generalized clonic convulsions occurred. He became drowsy, sank into a deep stupor with Cheyne-Stokes respiration and died June 11, with a terminal picture of uremia. Chemical analysis of the blood on the last day of life showed a urea nitrogen content of 133 and a creatinine content of 10.75 mg. per hundred cubic centimeters.

At postmortem examination (Dr. R. H. Jaffé) the pericardial sac extended from the right costochondral junction to the left midaxillary line and compressed the left lower lobe of the lung. The heart weighed 750 Gm. The left ventricle measured 20 mm. and the right ventricle 18 mm. The myocardium was firm and a light purplish brown. The apex was formed by the right ventricle. The epicardium was smooth and shiny. The

left auricle was slightly dilated and the thickness of the wall measured 1 mm. The foramen ovale measured 6 mm. in the longitudinal and 3 mm. in the greatest transverse diameter. It was covered by a fold which overlapped the opening completely. The mitral valve was of normal configuration.

In the uppermost portion of the interventricular septum there was a crescent-shaped defect 30 mm. in transverse and 12 mm. in vertical diameter. This defect, which was located opposite the anterior cusp of the mitral valve, led into the pulmonary conus and formed the only outlet of the left ventricle.

The aorta originated from the right ventricle and measured 120 mm. in circumference. The aortic valve had four leaflets; about the middle leaflet the left coronary artery originated, while about the right leaflet the right artery originated.

The pulmonary artery was located to the left and posteriorly to the left leaflet of the aortic valve. The pulmonary artery extended into the right ventricle for a distance of 3 cm. as a constricted tube lying on the right ventricular surface of the interventricular septum close to the anterior origin of the latter. The pulmonary ostium was thus about 3 cm. below the level of the aortic valve leaflet attachments and the opening was constricted to a circumference of 3 cm., as was the intraventricular portion, but then it widened to 53 mm. in circumference. The pulmonary artery was thin walled, with a smooth intimal lining. The pulmonary valve had two leaflets which were fused together to form a circular fold, which was evidently incompetent. The right auricle was markedly dilated, about 8.5 cm. in transverse diameter. The tricuspid valve was of normal configuration.

The lungs were moderately distended and subcrepitant. The main pulmonary artery was of normal configuration. On section it was a purple-gray and moderately moist. There were scattered fatty plaques in the pulmonary artery. On microscopic section no difference was noted in caliber between the branches of the pulmonary artery and the bronchial arteries.



Fig. 5.—Anterior view showing right ventricle and right aorta. Note the thickness of the right ventricular wall. The greatly dilated first portion of the aorta with the great vessel branches derived from this portion.

The kidneys weighed 225 Gm. and were moderately firm, and the capsule stripped with ease. The surface was a light purple-gray and uniformly granular. The granules were of pinhead size. The cortex measured 7 mm. and was purplish gray, but the markings were distinct. Microscopic examination of the

kidney sections revealed that the majority of glomeruli were completely or partially hyalinized. The remaining glomeruli were large and very cellular with the capsular space often obliterated. Many of the tubuli contorti were atrophic with a corresponding increase in the interstitial tissue. The granules were composed of hypertrophic tubules, the lumen of which was wide and the lining of which was cuboidal and finely granular. The larger arteries showed hypertrophy of the media, while the wall of the afferent and intralobular arterioles was slightly thickened. Sudan III stain revealed much fatty material, chiefly in the stroma in the form of nests of large cells filled with fat droplets. There was also some fat in the epithelium of some of the convoluted tubules and in the hyalinized glomeruli.

The complete anatomic diagnosis was chronic glomerulonephritis, detorsion defect of the large arteries of the heart with the origin of the aorta and pulmonary artery from the right ventricle, stenosis of the pulmonary ostium, defect of the interventricular septum, patent foramen ovale, hypertrophy of

men ovale was slitlike and covered by a fold, so that in all probability it was functionally closed. The development of the conus arteriosus was clearly demonstrated by the side to side position of the aorta and pulmonary artery, with complete coats, however, separating these vessels. The first portion of the aorta was evenly dilated and the major blood vessels came directly from this enlarged sac. The arch was poorly developed and the aorta, after leaving this saclike first portion, was comparatively small and narrow, measuring 40 mm. in diameter in the second portion and 36 mm. in diameter in the third portion.

#### SUMMARY

In an unusual case of the tetralogy of Fallot in a laborer who lived to his forty-first year, the second longest history in the literature, the clinical diagnosis was established according to Fallot's original descriptions. It is the only case of its kind which has come to autopsy in the records of the Cook County Hospital, where congenital heart disease of all types represents only 1 per cent of the postmortem material. The senior author, who has had a long association with this institution, has seen only one other adult<sup>18</sup> with congenital heart disease who lived longer than the patient in the present instance. The cause of death in our case was not due to any cardiac disturbance or dysfunction but to the uremic syndrome on the basis of chronic glomerulonephritis.

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Fig. 6.—Posterior view of the heart with the right auricle and ventricle open. Glass rod through the slitlike interauricular septum defect.

both ventricles of the heart, especially the right, marked dilatation of the right auricle of the heart, slight atheroma of the aorta and the coronary arteries, passive congestion and edema of the lungs and compression atelectasis of the left lower lobe of the lung, marked hydropericardium and slight ascites and bilateral hydrothorax, slight edema of the brain, nodose goiter and prostatolithiasis.

#### COMMENT

The slight degree of disability which this patient demonstrated during life can probably be explained by several points: First, the interventricular septal defect was so located that the direction of the blood current from the left ventricular contraction was apparently directed into the aortic opening. Second, the mouth of the pulmonary artery was in the right ventricle, as this artery was intraventricular for about 3 cm. As this pulmonary ostium was just below and anterior to the interventricular septal defect, right ventricular contraction forced blood into the stenosed pulmonary artery opening rather than through the septal defect. The patent fora-

### Clinical Notes, Suggestions and New Instruments

#### BENIGN GRANULOMA OF THE NOSE (SO-CALLED SARCOID)

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Sarcoid cannot be considered a rare disease. It is, however, of considerable interest in that marked variations in clinical manifestations may occur, and it offers considerable difficulty in diagnosis in differentiating tuberculosis, syphilis and other types of proliferative granulomas.

There are several outstanding facts in the manifestations of sarcoid. The sites of particular involvement are the skin and the lymph nodes, more particularly the superficial lymph nodes; but the mediastinal lymph nodes may show massive involvement. The bones involved are most frequently those of the extremities, especially the smaller bones, where frequently destructive lesions are present. The long bones also may be involved. In a review of the literature almost every part of the body has been mentioned as being involved in this process, and while we have found reference made to involvement of the nasal bones<sup>1</sup> we have not encountered a report of involvement of the nasal mucosa.

The lesion histologically<sup>2</sup> is a granuloma composed of collections of epithelioid cells which occasionally surround giant cells of the foreign body type. There is rarely any necrosis. Tubercle bacilli are not found. The cutaneous test is almost uniformly negative.

Clinically the course is of a benign prolonged character and some lesions may progress while others are retrogressing.

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There may be any combination of involvement, and the various syndromes described are purely clinical differentiations.<sup>3</sup>

From the standpoint of etiology, no single organism has been found to be present. A preponderance of evidence favors tuberculosis. Etiologic factors have been given also as leishmaniasis and leprosy; these seem unlikely. The finding of the

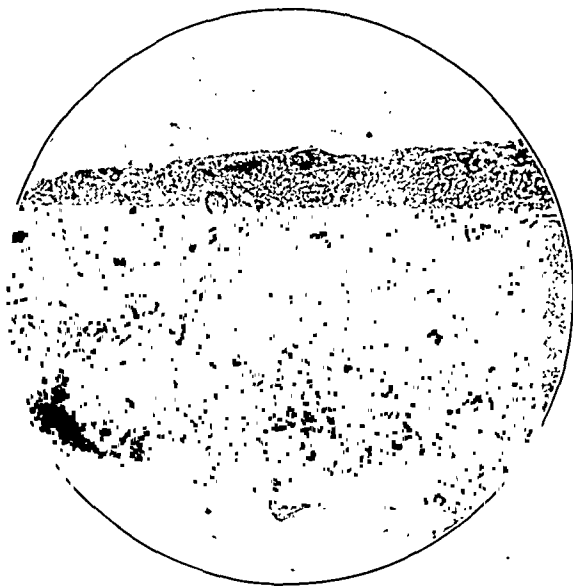


Fig. 1.—Section showing the thickness of the entire mucous membrane. Tubercle-like lesions are scattered throughout among the glands. Giant cells are found at the center of some of the tubercles. The latter are clusters of epithelioid cells radiating out from the center.

picture of hyperplastic tuberculosis with multiple tubercles without the presence of polymorphonuclear neutrophils and necrosis, without the finding of tubercle bacilli in cultures and

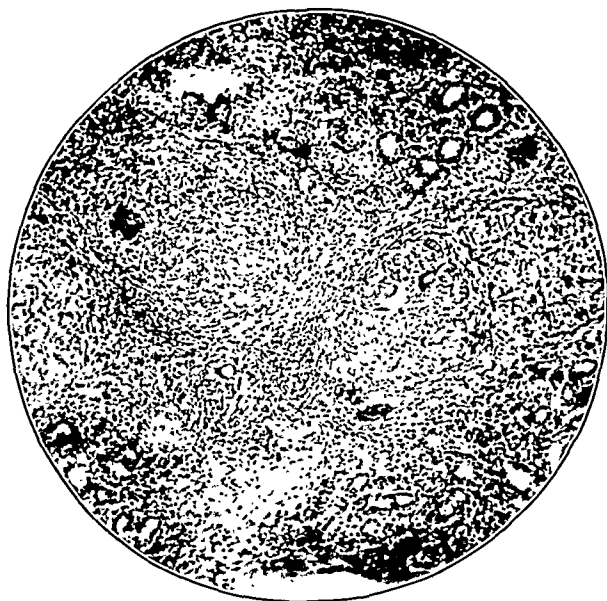


Fig. 2.—Section under higher power showing in more detail the characteristics of the tubercle-like lesions with their giant cells. Round cells and plasma cells are present, but there are no polymorphonuclear neutrophils, and no caseation necrosis is present.

in guinea pig inoculation and the negative cutaneous reaction for tuberculosis makes a diagnosis of sarcoid. It had probably better be termed granuloma of unknown etiology.

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#### REPORT OF CASE

A widow aged 50 presented herself for the first time in December 1930 complaining of nasal obstruction of several years' duration. In January 1931 we did a submucous resection of the septum and removed the cystic middle turbinate. At the time of the original examination she said that she felt there was a lump coming on the left side of her nose but was not sure, since the nose had always been a little broad and asymmetrical. Nasal breathing was satisfactory after the submucous resection. She returned in May 1932, sixteen months after the operation on the septum. At this time she showed definite infection of both antrums. She again remarked that she felt that her nose was enlarging but could not be sure that there was any material change. The x-ray laboratory reported an increased density in both antrums, also that the nasal bones showed an unusual density, especially along the inferior margins. The Wassermann reaction was negative on this occasion and had been negative on the previous examination. The infection of the antrums did not improve under conservative treatment, and a bilateral Caldwell-Luc operation was done from which recovery was rapid and uneventful. The



Fig. 3.—Section showing the tubercle-like lesion among the osseous trabeculae of the nasal bone. The spaces between the trabeculae are widened by this fibroblastic and granulomatous tissue. There is a slight increase in the number of osteoblasts along the trabeculae of the bone.

drainage ceased and the function of the nose was satisfactory, but the aching across the upper part of the face continued. During the next two months we were sure that the nose was enlarging across the bridge, and material for biopsy was taken from the bone at the junction of the nasal bones and the ascending process of the superior maxilla, from the subcutaneous tissue and from the mucosa of the nose.

A summary of the pathologic report by Dr. Robertson was as follows: On cross examination the bony tissue appeared rather spongy and the mucosa was somewhat firmer than normal. It was pale. On microscopic examination sections of both the mucosa and the bone showed the presence of many discrete tubercle-like lesions scattered throughout. These consisted of clusters of epithelioid cells radiating out from the center, and in the center of some there was a giant cell. These giant cells occurred singly and showed a peripheral arrangement of the nuclei in the shape of a horseshoe. Some of the tubercles on close examination were seen to contain capillary blood vessels in which there were erythrocytes. No polymorphonuclear neutrophils were present. There were lymphocytes in the surrounding tissue. It seems that the tubercle-like lesions in places were juxtaposed to blood vessels, and the blood vessels seemed somewhat narrowed. There was a suggestion

of central necrosis in some of these tubercles, but this was not definite and at no place was there anything that had the appearance of true caseation necrosis. In the bony tissue these tubercles occurred in the fibrous tissue among the bone trabeculae; there was evidence of active proliferation of the bone manifested by an increased number of osteoblasts along the

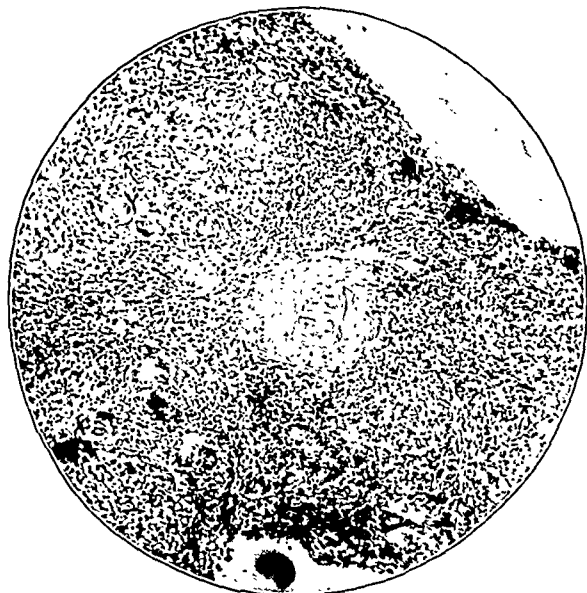


Fig. 4.—At the center is seen a thick-walled blood vessel with marked perivascular round cell infiltration and in the nearby vicinity there are several of the tubercle-like lesions. This was thought possibly to indicate syphilis.

trabeculae. Bacterial stains failed to reveal any bacteria of any type. Spirochete stains were not made.

On the basis of a distinct granulomatous process, which was principally proliferative and appeared to be somewhat perivascular without caseation necrosis, it was thought that this might possibly be syphilis in spite of the fact that the Wassermann reaction was consistently negative. It was on this basis that a therapeutic trial of antisyphilitic treatment was given.

Sections of the mucous membrane of the antrum did not show any evidence of the granulomatous process. The pathologic diagnosis was chronic sinusitis.

On the basis of the pathologic report the patient was put on antisyphilitic treatment consisting of intermittent courses of neoarsphenamine and thiobismol from September 1932 until March 1935. The only positive improvement during this time was relief from the aching pain in the face. The enlargement of the nose was insidiously progressive.

During the spring of 1936 there appeared a discoloration of the skin of the nose, and the opinion of a dermatologist was sought. Following is the report of Dr. Lyle B. Kingery: "Dermatologic examination reveals a purplish, plaque-like infiltrative process involving the skin of practically the entire nose. The process presents a firm consistency, is painless and devoid of acute inflammatory symptoms. It is fairly well demarcated and macroscopically presents no epidermal changes. In addition, both inspection and palpation impressed me with the fact that there is a productive change involving the underlying structures, particularly at the juncture of the nasal bones with the superior maxilla. Pressure reveals this to be painless, hard and fairly regular.

"The presence of the purplish infiltration, the absence of general health impairment, the slow progress over an extended period of time and the location of the process all point to a diagnosis of sarcoid. While this is not common, there is apparently sufficient evidence of occasional bony involvement to make this a part of the picture. Finally, in talking with Dr. Robertson, I was pleased to have him state that this diagnosis was acceptable to him in a reconsideration of the results of his biopsy."

At Dr. Kingery's suggestion the patient was treated with x-rays and given solution of potassium arsenite and weekly injections of bismuth salicylate. These were continued with intermissions until June 1937, when all treatment was stopped. There had been a decided improvement, and we hoped the growth had been arrested. When she returned for examination in September it was discouragingly evident that the process had become active again and the treatment was resumed. To date there has been no improvement, but for the last three months the process has remained stationary.

#### SUMMARY

We have just reported a case of sarcoid or, better termed, benign granuloma of unknown etiology, involving the nasal mucosa, nasal bones and overlying skin. The considerable difficulty in arriving at a final diagnosis was encountered because of the unusual involvement of the nasal bones and nasal mucosa. With the involvement of the overlying skin Dr. Kingery uncovered the true nature of the disease process and a review of the sections confirms his interpretation.

1130 Southwest Morrison Street.

#### GANGLIONEUROMA OF THE OVARY

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MEMPHIS, TENN.

Tumors composed of such highly specialized tissue as adult ganglion cells and their processes are comparatively rare. McFarland,<sup>1</sup> who reported a case in 1931, was able to find



Fig. 1.—Ganglioneuroma of the ovary. Posterior view of the lobulated, soft, epithelial covered tumor. The parenchyma is yellow-pink, juicy, translucent, very vascular, extremely soft and easily picked away. The tube is shown above.

reference in the literature to ninety-three similar tumors. The literature was likewise reviewed in 1932 by Bigler and Hoyne,<sup>2</sup> who added two cases of their own.

From the Department of Pathology, University of Tennessee Pathological Institute.

We are indebted for the illustrations in this study to Dr. Joseph L. Scianni, Artist, University of Tennessee Pathological Institute.

1. McFarland, Joseph: Ganglioneuroma of Retroperitoneal Origin, Arch. Path. 11: 113 (Jan.) 1931.

2. Bigler, J. A., and Hoyne, Archibald: Ganglioneuroma: Report of Two Cases with Review of Literature, Am. J. Dis. Child. 44: 1552 (June) 1932.

Loretz<sup>3</sup> reported the first instance in 1870. Since then ganglioneuromas have been reported as arising in the central nervous system, cranial nerve roots and their associated ganglions and the sympathetic ganglions of the neck, thorax and abdomen. They also may arise in the adrenal medulla, the carotid gland, the coccygeal gland and Zuckerkandl's organ. No previous report has been found of a ganglioneuroma arising in the ovary.

Ganglioneuromas appear to arise chiefly from the sympathetic nervous system. In the ovary, groups of sympathetic ganglion

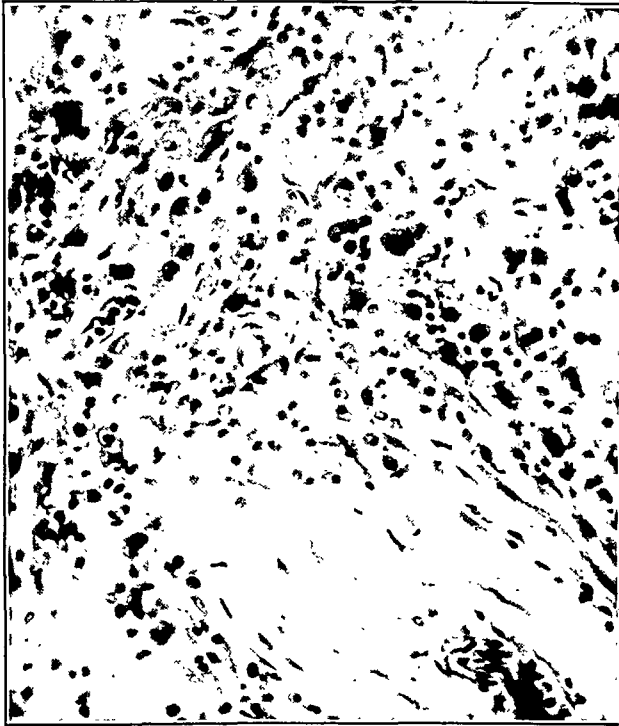


Fig. 2.—Section of ganglioneuroma of the ovary,  $\times 300$ . The stroma is very loose and rich in serum, with numerous delicate capillaries. The cells vary in size and shape, consisting of ganglion cells, polymorphonuclears and plasma cells. On the right, above and below are nerve fibers composed of pale, fine, wavy fibrils with elongated fusiform nuclei.

cells occur normally in the medulla near the hilus. Ewing<sup>4</sup> suggests that in cases presenting ganglioneuroma there is some "embryonal disturbance of the structure of the sympathetic nervous system, with the presence of superfluous undifferentiated tissue in localities giving origin to the tumors." This view is favored by their appearance so frequently in early life or as congenital tumors and by the fact that they are frequently multiple. That some of these tumors may begin as undifferentiated or embryonal types and later differentiate into a more adult type of ganglioneuroma is evident from the case reported by Cushing and Wolbach.<sup>5</sup>

A ganglioneuroma is usually a firm, circumscribed, nodular pale tumor which may be small or large. The microscopic appearance is distinguished by the presence of characteristic adult ganglion cells with their processes. The proportion of neurofibrils present is variable.

#### REPORT OF CASE

**History.**—R. B., a Negro girl aged 4 years, was admitted to the surgical service of Dr. F. W. Smythe at the John Gaston Hospital, April 11, 1935, because of painful swelling of the abdomen which had been noted for three weeks. This had become progressively worse and for two days before admission was accompanied by an edematous swelling of the legs.

Physical examination showed that the child was normally developed and well nourished. The abdomen was distended and occupied by a freely moving mass extending out of the pelvis to a level just above the umbilicus. The mass was fairly firm and smooth but with palpable depressions on one edge. It was not tender. Roentgenographic studies indicated that the mass was not associated with the kidney or intestine. The other physical changes were noncontributory.

Roentgen irradiation with 1,500 roentgens within nine days was given. Laparotomy was then performed and the mass excised, along with the attached right ovary and the fallopian tube. An uneventful convalescence followed.

**Pathologic Report.**—The specimen consisted of a lobulated, soft mass weighing 200 Gm., covered with tunica albuginea. Along its summit ran the fallopian tube. On section the tissue was everywhere yellow-pink, juicy, translucent, very vascular, extremely soft and easily picked away (fig. 1).

Microscopic examination showed a thin peripheral layer of ovarian tissue. Underlying this the normal ovarian structure was completely replaced by a tissue whose stroma was very loose and for the most part appeared to be composed of serum. There were many delicate capillaries. The cells varied in size and shape, but the general type was a large multipolar cell with a basophilic, finely granular cytoplasm. The nucleus was large, round or oval, light staining and reticulated and had in it a large, prominent, densely staining nucleolus. The typical cell was tripolar, with processes from its poles, some of which could be followed for short distances into the stroma. These cells bore a striking resemblance to a typical ganglion cell. A large proportion of these larger cells were multinucleated;



Fig. 3.—Section of ganglioneuroma of the ovary,  $\times 725$ , center of figure 2. Scattered loosely through the fluid-filled, practically fibrous tissue-free stroma are large multipolar ganglion cells with basophil, finely granular cytoplasm and large, round or oval, light staining and reticulated nuclei with large, prominent, densely staining nucleoli. A typical tripolar ganglion cell with processes from its poles can be seen in the center, and a delicate capillary on the left below. Several ganglion cells contain two or three nucleolated nuclei. Plasma cells and polymorphonuclear leukocytes are also seen.

the majority contained two well formed nucleolated nuclei as described at opposite poles of the cell or beside one another. Some of the cells contained three nuclei. The variations in the cells consisted in the amount and shape of the cytoplasm,

3. Loretz: Ein Fall von gangliösen Neurom, Virchows Arch. f. path. Anat. 49: 435, 1870.

4. Ewing, James: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1928, p. 471.

5. Cushing, H. S., and Wolbach, S. B.: Am. J. Path. 3: 203 (May) 1927.

but the nuclei were essentially the same. The cell shapes ranged from round ones the size of a large mononuclear with one process to fat fusiform ones with a process at each end. Some of the cells showed a single large vacuole in the cytoplasm. A number of the larger cells showed a single, large, pink staining hyaline droplet in their cytoplasm, or the whole cell body was filled with hyaline droplets ranging in size from that of a large red blood cell to fine droplets. An occasional mitotic figure was found in a ganglion cell. The cells were either scattered loosely and indiscriminately through the fluid-like stroma or were massed in large poorly demarcated clumps. In the center of these larger denser fields some pale, fine, wavy fibrous bundles with wavy, elongated, deep staining fusiform nuclei were present. These bundles were frayed at their ends and suggested nerve fibers. The section was practically free of fibrous tissue. A striking feature of the whole section was the presence of large numbers of plasma cells and mature polymorphonuclear cells, about equal in number, which were indiscriminately infiltrated throughout the section with no suggestion of clumping or localization (figs. 2 and 3).

## SUMMARY

A ganglioneuroma of the ovary occurring in a Negro girl aged 4 years consisted of adult ganglion cells and fibrils mixed with some less differentiated elements. No previous report of a ganglioneuroma of the ovary has been found in the literature.

## TRAUMATIC THROMBOSIS OF DEEP PALMAR VEIN

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AND

WILLIAM H. SNYDER JR., M.D.  
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There has been a good deal of literature devoted to injuries to the hand and their economic significance in industry. Discussions of infections, injuries to tendons and nerves and fractures form the bulk of the articles, but reports of injuries to blood vessels appear from time to time. There have been

several cases of aneurysm<sup>1</sup> reported and one case of thrombosis of the ulnar artery<sup>2</sup> following a blow.

No case of traumatic thrombosis of the deep veins of the palm of the hand could be found in the literature, so we felt it worth while to report such a case. The thrombosis was the result of a sudden severe jar at the base of the hand. A definite, firm, tender, oblong mass could be palpated at the

base of the hypothenar eminence (fig. 1). It was thought to be a ganglion or chronic tenosynovitis, but exploration revealed a thrombosed deep ulnar vein and fourth digital vein (fig. 2).<sup>3</sup>

Operative removal resulted in relief of pain in the palm and made it possible for the patient to return to work as a blacksmith within three weeks.

The patient was a man of stable temperament whose story could be relied on.

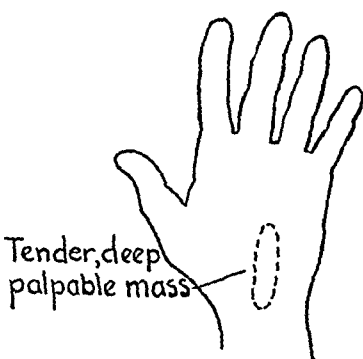


Fig. 1.—Position of palmar mass on left hand.

base of the hypothenar eminence (fig. 1). It was thought to be a ganglion or chronic tenosynovitis, but exploration revealed a thrombosed deep ulnar vein and fourth digital vein (fig. 2).<sup>3</sup>

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The patient was a man of stable temperament whose story could be relied on.

1. Regnault, J., and Bourrat-Lacoutur, H. E. L.: *Anévrysme professionnel de l'arcade palmaire superficielle*, *ev. de chir.* 47: 337, 1913. Rastouil and von Robineau: *Bull. et mém. Soc. de chir. de Paris* 38: 15 (No. 1) 1913.

2. von Rosen, Sophus: *A Case of Thrombosis of the Ulnar Artery After an Injury with a Blunt Instrument*, *Acta chir. Scandinav.* 73: 500-506, 1934.

3. Toldt, Carl: *An Atlas of Human Anatomy: Anatomy of Veins of the Palm*, ed. 2, New York, Rebman Company 2: 700, 1926.

## REPORT OF CASE

A man aged 67, a blacksmith, about a month before consulting a physician was holding an anvil while it was being pounded on, and a sudden jar caused immediate pain in the palm of the left hand. Since that time he had experienced considerable pain whenever he used that hand. A mass appeared at the site of the injury soon afterward. The ring finger became so painful that he could not move it without discomfort. Pressure

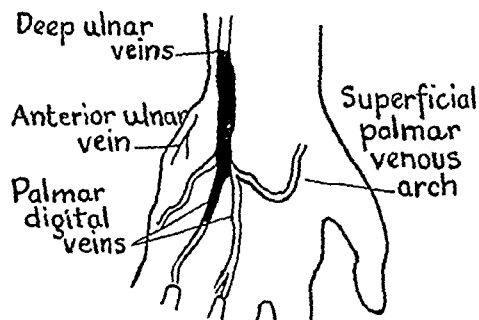


Fig. 2.—Veins of palm of left hand, showing portion thrombosed.

of any kind on the palm caused pain. He padded and bandaged it but still had difficulty in using his hand. He did not stop work, however, thinking that the condition would improve of its own accord in time. After four weeks, during which time the pain made him entirely unable to carry on his work satisfactorily, he consulted a physician.

His past history and family history were entirely irrelevant. He was well nourished and well developed, appearing robust for his age. There were no conditions noted of any significance except for scars on his arms of many previous injuries incident to his work. None had been of a serious nature. On examination of the left hand, the palm at the base of the hypothenar space was tender. A mass was palpable below the surface, apparently in the muscle bundle, measuring about 1 by 2.5 cm. It was firm and movable but did not move with flexion and extension of the fingers. No surface lesion could be seen. There was slight diminution in sensation in the fourth and fifth fingers on the palmar aspect.

Dr. Steele F. Stewart, called into consultation, described the lesion as follows: "There is a small deep elastic mass near the base of the hypothenar eminence of the left hand which appeared following trauma one month ago. It is slightly tender

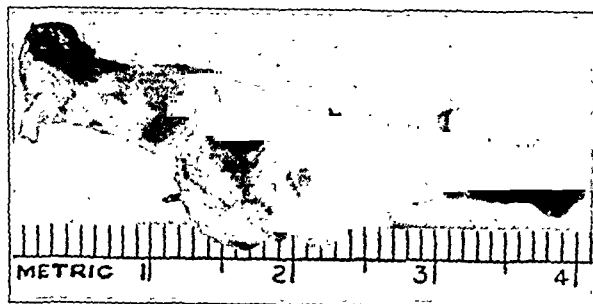


Fig. 3.—Thrombosed vein of hand removed at operation.

and appears to be along the tendons of the fifth finger. My impression is that it is a tenosynovitis, post-traumatic, which interferes with use of the finger and hand. I think that long rest will let it disappear but that surgery will hasten the process." The surgeon's diagnosis was "ganglion" of the left palm.

It was decided that surgery should be resorted to to put the man back to work as soon as possible.

Operation was done under local procaine hydrochloride anesthesia by injection into the median and ulnar nerves just above

the wrist and a cuff anesthesia by infiltration around the wrist. Incision was made in the palm of the left hand beginning just distal to the wrist and following the middle crease of the palm for a distance of about 3.5 cm. The palmar skin was then dissected back, the palmar fascia exposed and a mass palpated directly beneath the palmar fascia. The fourth digital nerve branching from the ulnar nerve was then exposed just beneath the fascia and dissected free from the mass. The mass was found to originate from the fourth digital vein and extended upward within the deep ulnar vein 3.5 cm. to the wrist. It consisted of a dilated vein with thrombosis. The vein was clamped and tied at both ends and removed. The subcutaneous tissues were brought together with interrupted plain catgut. The skin was closed with interrupted dermal mattress sutures. The postoperative diagnosis was thrombosis of the fourth digital vein and the deep ulnar vein in the hand.

The specimen (figs. 3 and 4) was a greatly dilated vein measuring 0.4 cm. in thickness. In its midportion there were two little nodules measuring 1 by 0.6 cm. The microscopic



Fig. 4.—Cross section of thrombosed vein of hand showing beginning organization of clot.

section showed a thickened fibrous venous wall with antemortem clot which was quite firmly adherent in places. The pathologic diagnosis was dilatation and thrombosis of a small vein.

The patient made an excellent recovery and was able to return to active duty three weeks after the operation. He is now free from pain and is using his hand normally.

#### SUMMARY

An injury resulted in thrombosis of the deep ulnar and fourth digital veins of the palm of the left hand. A small, deep, palpable, tender mass was present at the base of the hypothenar eminence. The question of prolonged rest for the cure of a chronic tenosynovitis was considered but rejected in favor of exploration. At operation a greatly dilated small thrombosed vein was removed and the patient was able to return to work soon after.

This is the first case we can find reported in the literature of traumatic thrombosis of a deep palmar vein and we hope that this presentation will be of some help in the diagnosis of similar cases in the future.

6777 Hollywood Boulevard.

#### THE PHOTOSTETHOSCOPE

A DEVICE FOR VISIBLY DEMONSTRATING CARDIAC SOUNDS,  
ESPECIALLY FETAL HEART SOUNDS

EDWIN J. DE COSTA, M.D., CHICAGO

Knowledge of the condition of the fetus in utero is entirely dependent on observation of the fetal heart tones. Methods of observation have varied as science has progressed and made available new instruments. Fetal heart tones were first heard with the unaided ear in 1818 by Major.<sup>1</sup> It was not long before the newly invented stethoscope was also put into use. That the stethoscope itself was not a great advance is proved by the frequency with which one encounters direct auscultation, even at the present time. Later the head stethoscope was introduced, making it possible for the obstetrician to observe the heart tones without interfering with asepsis. However, at best it is an awkward, uncomfortable instrument.

With the improvement of electrical means of reproducing, transmitting and amplifying sound waves, it was inevitable that such methods should be applied to the study of adult and fetal heart sounds. In 1923 Falls and Rockwood<sup>2</sup> published a preliminary report on the use of microphonic reproduction of fetal heart tones. They employed the instrument demonstrated by Abbott at Purdue University in 1922.<sup>3</sup> In this preliminary report they mention certain difficulties encountered, most serious of which arose from extraneous noises and feed-back howls. They believed that if these difficulties could be eliminated the machine would become standard equipment in every maternity hospital. The problems they faced in 1923 are still met today, in spite of the tremendous improvement in microphones, thermionic valves and amplifying and reproducing apparatus. Electric stethoscopes are available commercially for the auscultation of adult heart tones and for the demonstration of fetal heart tones, but they are not entirely satisfactory. The most recent type of amplifying stethoscope is that described by Matthews.<sup>4</sup> In order to overcome the aforementioned difficulties, his model has become such a complicated, cumbersome and expensive piece of equipment that the author himself admits it to be unpractical even for hospital use.

The present study is concerned with the development of a simple, compact and inexpensive device that will demonstrate to the physician the condition of the baby as manifested by the heart tones. A sensitive transmitter of the crystal type and a high gain amplifier which satisfactorily amplifies fetal heart tones so that they can be heard several hundred feet away are so sensitive that the microphone picks up the sounds from the loud speaker and develops a howl. It has been impossible to filter out the feed-back and preserve simplicity and compactness. In this device the loud speaker has been eliminated entirely and a small neon lamp substituted; the device is called the photostethoscope. The photostethoscope translates sound into flickers of light and by this means reproduces the rate and regularity of fetal heart sounds quite as faithfully as the speaker. The greatest nuisance—feed-back—is eliminated.

The photostethoscope is housed in a small metal cabinet from which extend leads to the microphone and power line. The microphone, supported by sponge rubber, is attached by a wide adhesive strip to that location of the abdomen where fetal heart tones are most audible. Electrical connection is established through any wall plug. The gain control (A) is then adjusted to attain the degree of amplification necessary to operate the indicating bulb (B). Either the first or the first and second fetal heart sounds may be demonstrated as flickers of light by varying the gain adjustment.

The microphone, on its rubber cushion, causes no discomfort to the patient. During labor it need not be in constant applica-

1. Major, quoted in *Bibliothèque universelle de Genève*, November 1818.

2. Falls, F. H., and Rockwood, A. C.: Use of Microphonic Stethoscope in Demonstration of Fetal Heart Tones, *J. A. M. A.* 81: 1683-1684 (Nov. 17) 1923.

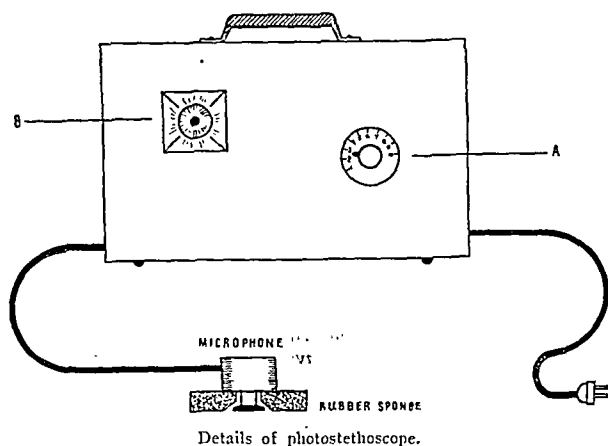
3. Abbott, R. B.: Eliminating Interfering Sounds in a Telephone-Transmitter Stethoscope, *Physiol. Rev.* 21: 200 (Feb.) 1923. Keiper, G. F.: A Multiple Electrical Stethoscope for Teaching Purposes, *Correspondence*, *J. A. M. A.* 81: 679 (Aug. 25) 1923.

4. Matthews, H. B.: The Continuous Auscultation of the Fetal Heart by Means of an Amplifying Stethoscope, *Am. J. Obst. & Gynec.* 34: 898-899 (Nov. 1937).

tion but can be held against the abdomen as frequently as desired. During delivery the microphone remains constantly in place and in no way interferes with the aseptic technic.

There are some minor defects. Strong uterine contractions interfere with the operation of the apparatus for the duration of the pain, but with relaxation the heart tones are again demonstrable. Fetal movements and shifting of the linen produce arrhythmic flickers of light; slight changes in the draping technic will minimize the disturbance from this source. Extraneous sounds, caused by walking or talking in the labor room, interfere only when they are loud, but crying or snoring by the patient creates a more serious annoyance. The vibration is apparently transmitted through the delivery table to the microphone. This annoyance can be greatly reduced by using a sponge rubber mattress on the delivery table and securing the cooperation of the patient. The most serious source of interference is from unshielded, high voltage x-ray equipment. Proper shielding and grounding of such x-ray apparatus constitute the only satisfactory method of eliminating such disturbance.

It is safer to install the amplifying unit outside the delivery room when gaseous anesthetics are used. For this the microphone cord can be lengthened and the indicating lamp may be mounted in the delivery room. There is nothing in the amplifier to spark or arc, but a breakdown of the condenser might be a hazard.



These objectionable factors are not always present. In any event they are outweighed by the positive advantages. The facility of application of this instrument encourages its frequent use. The continuous portrayal of fetal heart tones presents constant information concerning the condition of the fetus. With such information available, failure to recognize imminent intrapartum death should occur less frequently.

The photostethoscope may prove useful in the study of abnormalities of the adult heart. Enough work has been done to indicate definite light patterns associated with murmurs and the various arrhythmias. It affords a new avenue of approach for studying the heart and provides an additional method of demonstrating cardiac action to students.

#### SUMMARY

The photostethoscope is a practical, efficient and inexpensive device for demonstrating fetal and adult cardiac sounds. It was designed for the continuous observation of fetal heart tones during second stage labor and delivery. Fetal distress can be promptly detected by its use.

1540 East Fifty-Third Street.

**The First European Asylum.**—The first European asylum devoted exclusively to the care of the insane of which we have indisputable record was that built at Valencia, Spain, in 1408 by Fray Gope Gilaberto. A number of other asylums were established in various other parts of Europe during the sixteenth century.—Deutsch, Albert: *The Mentally Ill in America*, New York, Doubleday, Doran & Co., Inc., 1937, p. 16.

## Special Clinical Article

### EVALUATION OF THE INJECTION TREATMENT OF HERNIA

A STATISTICAL AND ANALYTIC STUDY

CLINICAL LECTURE AT SAN FRANCISCO SESSION

FRANKLIN I. HARRIS, M.D.

AND

ALFRED S. WHITE, M.D.

SAN FRANCISCO

The treatment of hernia by injection has been a controversial subject for over a hundred years. Until recently there was an overwhelming skepticism as to the safety and value of this method. In the last five years this skepticism has been replaced by an enthusiasm which has resulted in its widespread use. Optimistic reports have appeared similar to those of the late Ignatz Mayer<sup>1</sup> of Detroit and Franz Wyss<sup>2</sup> of Switzerland, who claimed a cure in 96 per cent of their cases by the injection method. Bratrud,<sup>3</sup> McKinney,<sup>4</sup> Rice<sup>5</sup> and McMillan and Cunningham<sup>6</sup> reported cures in from 83 to 92 per cent of their cases. In contrast to such results, Burdick and Coley<sup>7</sup> of New York submitted statistics showing unsuccessful results in 96 per cent of their cases. Many surgeons when interviewed emphatically state, without quoting any personal experience, that the injection method is theoretically unsound and unsafe and from the practical standpoint is worthless in the treatment of hernia.

An endeavor to evaluate this method was approved by the research committee of the Mount Zion Hospital, San Francisco, in February 1934. A planned and systematic investigation of the treatment of hernia by the introduction of irritant chemicals into fascial planes was begun. Experimental animals were used for study of the reactions of the proliferative tissue to various solutions, and the biochemical properties of such solutions were critically analyzed. A scientific study of the construction and application of trusses was made, and a special hernia clinic was established in the outpatient department. A careful, detailed recording and follow-up system was instituted, from which 23,000 items were analyzed for this report. We treated the patients ourselves. All clinical observations were made with the attitude of comparing the results with those for years obtained with our operative treatment of rupture.

During the past few years we have submitted progressive reports of this work.<sup>8</sup> It is our purpose in this paper to present certain definite conclusions which

From the Department of Surgery, Mount Zion Hospital.  
Read in the Surgical Section of the General Scientific Meetings at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 14, 1938.

1. Mayer, Ignatz: Treatment of Inguinal Hernia by Subcutaneous Injections, *M. J. & Rec.* **131**: 90 (Jan.) 1930.
2. Wyss, Franz: Treatment of Inguinal Hernia by Alcoholic Injections, *Schweiz. med. Wchnschr.* **59**: 85 (Jan.) 1929.
3. Bratrud, A. F.: The Ambulant Treatment of Hernia, *Ann. Surg.* **105**: 324 (March) 1937.
4. McKinney, F. S.: An Evaluation of the Results of the Injection Treatment of Inguinal Hernia, *Ann. Surg.* **105**: 338 (March) 1937.
5. Rice, C. O.: The Injection Treatment of Hernia, *Ann. Surg.* **105**: 343 (March) 1937.
6. McMillan, W. M., and Cunningham, D. R.: The Injection Treatment of Reducible Hernia, *J. A. M. A.* **106**: 1791 (May 23) 1936.
7. Burdick, C. G., and Coley, B. L.: Injection Method of Treating Hernia, *Ann. Surg.* **106**: 322 (Sept.) 1937.
8. Harris, F. I., and White, A. S.: The Injection Treatment of Hernia, *Surg., Gynec. & Obst.* **63**: 201-211 (Aug.) 1936; The Injection Treatment of Hernia: Its Experimental Basis, *California & West. Med.* **45**: 382-385 (Nov.) 1936.



we believe will reconcile the wide divergence of opinion which has existed as to the value of the injection method of treating hernia.

From 1933 to 1938, 573 patients with hernia of all types have presented themselves for treatment (table 1). Of this number 236, or 41 per cent, were treated by the injection method, ninety-one, or 16 per cent, by operation, and 246, or 43 per cent, by the

TABLE 1.—Type of Treatment According to Diagnosis in Total Series (573 Cases)

Type of Hernia	Injection	Surgical	Mechanical
Pure indirect inguinal.....	118	35	149
Combined indirect and direct inguinal..	39	14	19
Pure direct inguinal.....	33	10	21
Recurrent postoperative inguinal.....	29	4	17
Umbilical.....	5	5	14
Femoral.....	3	12	10
Ventral.....	9	11	16
Number.....	236	91	246
Percentage.....	41	16	43

TABLE 2.—Reasons for Not Using Injection Method

	Number of Cases	Percentage of Total Series
Hernia not reducible.....	38	6.6
Satisfactory truss could not be fitted.....	55	9.6
Patient preferred operation.....	53	9.4
Treatment not advised because of age or infirmity.....	39	6.8
Patient satisfied with truss wearing; refused any treatment.....	152	26.6
Injection used.....	236	41.0
Total.....	573	100%

application of trusses. Only 41 per cent of the cases could be utilized for this clinical investigation, despite the fact that in this especially established clinic for the study of the injection method we tried to treat as many patients as possible by this means. An analysis of the remaining 59 per cent of the cases shows the limitation of the possible application of this procedure (table 2).

From a study of table 2 it may be seen that in 6.6 per cent of the cases injection could not be considered because of lack of complete reducibility of the hernia, that in 9.6 per cent of the cases it could not be contemplated because of inability to fit a satisfactory truss, that 9.4 per cent of the patients preferred operation as an easier method of treatment and that 6.8 per cent of the patients were considered unsuitable for this method because of infirmity, old age or poor tissues. It is interesting that the mechanical method of relieving rupture by the simple application of a retaining truss was sufficient to satisfy the needs of 26.6 per cent of the patients referred to this clinic. In this paper we are interested primarily in a study of the 236 cases in which treatment was by the injection method.

The first conclusion derived from our experience is that this method of treatment has not been responsible for a single death. The complications which have occurred have been reported in detail elsewhere.<sup>9</sup> There has been no atrophy or sloughing of the testicles and no peritonitis or formation of abscess. No impotence has resulted. Complications such as transient swelling of the cord, hydrocele of the cord, epididymitis, tran-

sient shock due to intraperitoneal injection of the solution and dermatitis of the skin under the truss pad have all been of minor significance and have not required hospitalization in any case. Even these complications were noted mainly in our early experience.

We are convinced that in the hands of experienced surgeons familiar with the principles and technic the injection method is absolutely safe and devoid of serious complications. We are convinced that there is a place for this method in the treatment of hernia. We are also convinced, however, that the end results are not comparable to those obtained with surgical procedures. We are convinced that many of the published enthusiastic reports have not been subjected to sufficient critical analysis and follow-up. We believe that it is of the utmost importance to publicize to the medical profession and to the public exactly what can be expected in the way of permanent cures from the injection method.

We define a cure of a hernia as the complete absence of the protrusion on examination as well as the absence of any bulge in the musculature on straining. A cure also implies that the patient has no need to wear a mechanical device such as a truss. On the basis of this definition our figures show that 134 patients, or approximately 57 per cent of the total of 236, can be said to be cured. These patients have been examined from six months to three years after the removal of the truss

TABLE 3.—Present Status of Patients Treated by Injection

	Number of Cases	Percentage of Cases
Cures.....	134	56.8
Possible cures.....	66	27.9*
Known failures.....	36	15.3
	236	100%
Length of time since truss was removed after cured		
6 months to 1 year.....	32	24
1 year to 2 years.....	62	46
2 years to 3 years.....	40	30
	134	100%

\* Still wearing trusses.

TABLE 4.—End Results in Unselected Cases in Relation to Type of Hernia

Type of Hernia	Number of Cases	Number of Cures	Percentage of Cures	Number of Possible Cures	Percentage of Possible Cures	Number of Failures	Percentage of Failures
Pure indirect inguinal.....	118	96	81.4	11	9.3	11	9.3
Combined indirect and direct inguinal.....	39	15	39.1	19	48	5	12.9
Pure direct inguinal.....	33	9	26.8	17	52	7	21.2
Recurrent postoperative inguinal.....	29	6	21.5	15	52	8	27.5
Umbilical.....	5	5	100	..	..	..	..
Femoral.....	3	1	33.3	..	..	2	66.7
Ventral.....	9	2	22.6	4	44	3	33.4
	236	134	56.8	66	27.9	36	15.3

(table 3). Sixty-six patients, or 28 per cent, are listed as possibly cured. By this we mean that they are still wearing a truss, either because we advised them to or because they do not feel sufficiently secure to go without one. In this group there is no objective evidence of hernial protrusion, but the result can be classified only as a possible cure. The treatment of thirty-six patients

9. Harris, F. I., and White, A. S.: Injection Treatment of Hernia, *Am. J. Surg.* 37: 263 (Aug.) 1937.

has been classified as a complete failure, by which we mean either that we have been unable to obtain an initial closure or have been unable to cure a recurrence. This gives a percentage of complete failures of approximately 15. Table 4 contains a detailed statement of these figures according to the type of hernia.

This figure of 15 per cent failures, which represents our final figure to date, does not give a true picture of

TABLE 5.—Time of Recurrence After Last Injection

Number of Cases	Percentage of Cases	Time in Months
29.....	36.7	0-6
21.....	26.7	6-12
19.....	24.0	12-18
6.....	7.6	18-24
4.....	5.0	24-36

TABLE 6.—Causes of Recurrences and Final Failures

	Number of Recurrences	Number of Final Failures
Insufficient treatment .....	32	0
Improper truss .....	3	3
Refusal of patient to cooperate.....	8	8
Poor proliferative response.....	16	7
Obesity .....	6	4
Large size of hernia.....	2	2
Inability to hold hernia with truss due to pain .....	1	1
Inability to hold hernia with truss due to cough .....	2	2
Inability to hold hernia with truss, cause unknown .....	5	5
Sliding hernia .....	2	2
Discontinuance of treatment due to dermatitis from truss pad.....	2	2
	79	36

the actual recurrences. We found that many hernias remained closed for from six to eighteen months and then recurred (table 5). These hernias were those which early in our experience seemed to be closed after a few injections and were considered cured. The fallacy of discontinuing treatment on this basis was seen when frequent recurrences developed. This may explain the poor end results reported by surgeons who have not treated their patients over a sufficient period of time. The total number of such recurrences was seventy-nine, giving an immediate recurrence rate of 34 per cent. When further courses of treatment were given, fifty-six of the hernias were finally closed and are now included among those cured, while the remaining twenty-three were added to the list of complete failures. Thus an initial recurrence rate of 34 per cent was reduced to a final figure of 15 per cent failures by persistent retreatment.

The difficulties met in this form of treatment and the reasons for the recurrences and failures are illustrated by table 6. We note that most of the recurrences can be attributed to errors in technic, such as insufficient treatment or improper fitting of the truss. The final figure of thirty-six failures represents the minimum of failures due to the inherent inadequacy of the method.

Failure by the injection method does not preclude the possibility of cure by operative means or palliative treatment by truss wearing. Table 7 shows the final disposition of our failures, and it may be pertinent to note that operation on patients previously treated by injection has not in our experience been technically difficult. It is true that at operation there is some distortion of the usual lines of cleavage in the inguinal region, and a varying amount of fibrosis may be found.

Our operative experience in such cases has confirmed our experimental work on animals and has convinced us that the injection of irritant chemicals does produce binding adhesions between muscle and fascia.

In previous papers<sup>10</sup> we emphasized the fact that our patients with hernia were divided into two main groups, the good risk group and the poor risk group. In all fairness to the injection method we must analyze our figures again from this point of view. The good risk group is composed of patients who are good surgical risks; they are mainly under 50 or if over 50 have no serious organic disease that contraindicates operation. The poor risk group is composed largely of patients over 50 in poor general physical condition, and in our opinion its members were definitely never safe surgical risks (table 8).

There were, in the total series of 236 patients, 136 good risks. In this group 108, or 79.5 per cent, were cured; there were eleven, or 8 per cent, possible cures and seventeen, or 12.5 per cent, definite failures. In the poor risk group of 100 patients there were 26 per cent of cures, 55 per cent of possible cures and 19 per cent of definite failures. Despite the apparent small percentage of cures in the latter group, the general improvement in the comfort of the patient by reduction in the size of the hernia or by its complete elimination after the injection treatment makes the results satisfactory even though continued truss wearing is necessary.

Certain definite factors influence the results obtained. An analysis of table 9 shows that the relation of cure to the age of the patient is significant. The young patient has a better outlook for cure by the injection method than the older patient. This confirms the excellent results we recently reported in the treatment of hernia in children by the injection method.<sup>11</sup>

The length of time the hernia has existed (table 10) is also of considerable importance. The older the hernia the less chance of curing it, although there is

TABLE 7.—Disposition of Final Failures

Hernia present but $\frac{1}{4}$ to $\frac{1}{2}$ previous size and easily held by truss.....	14
Hernioplasty done .....	11
Patient not improved; operation to be done later.....	11
	36

TABLE 8.—End Results in Cases of Good and of Bad Risks

Result	Good Risk		Poor Risk	
	Number	Percentage	Number	Percentage
Cures.....	108	79.5	26	26
Possible cures.....	11	8.0	55	55
Known failures.....	17	12.5	19	19
	136	100	100	100

an excellent outlook for improvement to the point of possible cure.

The length of the inguinal ligament, which heretofore has been entirely overlooked in the differential diagnosis of the types of inguinal hernia, is likewise of primary importance. In our early investigations we

10. Harris, F. I., and White, A. S.: The Injection Treatment of Hernia: Its Present Day Status, California & West. Med. 45:391-395 (Nov.) 1936; Injection Treatment of Hernia, Proceedings of the Pan Pacific Surgical Association, July 1937.

11. Harris, F. I., and White, A. S.: The Injection Treatment of Reducible Inguinal Hernia in Children, Arch. Pediat. 54:665 (Nov.) 1937.

found that it was of the utmost necessity in injection therapy in contrast to operative treatment to make an exact differential diagnosis of the type of inguinal hernia. Our studies led to the development of certain definite differential points which heretofore have not been described. Most important of these points is the length of the inguinal ligament as measured from the anterior-superior spine to the spine of the pubis. In

TABLE 9.—Analysis of End Results in Relation to Age of Patient

Age of Patients, Years	Number of Cured Patients	Percentage of Cures	Number of Possibly Cured Patients	Percentage of Possible Cures	Number of Known Failures	Percentage of Failures
0-15	18	90.0	..	....	2	10.0
15-30	28	82.3	3	8.8	3	8.8
30-40	24	72.7	5	15.1	4	12.2
40-50	39	67.2	9	15.5	10	17.3
50-60	20	46.5	15	31.7	8	18.8
60-70	5	13.3	27	72.9	5	13.8
70-80	..	....	7	63.6	4	36.4
	134		66		36	

TABLE 10.—Analysis of End Results in Relation to Age of Hernia

Age of Hernia	Number of Cures	Percentage of Cures	Number of Possible Cures	Percentage of Possible Cures	Number of Failures	Percentage of Failures
0-1 year.....	81	76.4	10	9.4	15	14.2
1-2 years.....	23	74.2	6	19.3	2	5.9
2-5 years.....	12	38.7	7	22.6	12	38.7
5-10 years.....	12	44.4	14	51.9	1	3.7
Over 10 years..	6	14.6	29	70.8	6	14.6
	134		66		36	

a previous communication<sup>12</sup> it was shown that when the inguinal ligament measured less than 13 cm. the hernia was always of the pure indirect type, whereas when the length approximated 15 cm. the hernia was often found to be a combination of the indirect and the direct type. When the inguinal ligament was over 15 cm. the hernia was always of the pure direct type. Table 11 shows that the average length of the inguinal ligament in the cases in which cure resulted was 13 cm., whereas the average length in cases of possible cure and of failure was 15.2 cm. This shows the prognostic significance of the length of the inguinal ligament in the treatment of hernia by injection. Our unpublished studies lead us to believe that this measurement is of similar prognostic value in the operative cure of hernia.

With the foregoing figures and facts in mind, an evaluation of the injection method in unselected cases of hernia can be made as follows (table 12): With pure indirect inguinal hernia there is an 80 per cent chance of cure; with combined indirect and direct inguinal hernia there is only a 37 per cent chance of cure, while with pure direct inguinal hernia there is only a 30 per cent possibility of cure. Recurrent postoperative inguinal hernias show 22 per cent of cures. Reducible umbilical hernias in our experience have shown a 100 per cent chance of cure. These umbilical hernias were mainly in young children. Femoral and most incisional hernias are totally unsatisfactory for treatment by this method.

TABLE 11.—Length of Inguinal Ligament in Relation to End Results

Type of Hernia	Average Length of Inguinal Ligament		
	Cures	Possible Cures	Failures
Pure indirect inguinal.....	12.5 cm.	13.5 cm.	13.5 cm.
Combined indirect and direct inguinal.....	14.0 cm.	15.0 cm.	15.0 cm.
Pure direct inguinal.....	16.0 cm.	17.5 cm.	17.0 cm.
Recurrent postoperative inguinal.....	14.5 cm.	14.75 cm.	14.75 cm.
Average for cured group, 13.0 cm.			
Average for possible cures and known failures, 15.2 cm.			

TABLE 12.—Possibilities of Treatment in Unselected Cases of Inguinal Hernia

Type of Hernia	Approximate Result		
	Cures	Wearing Truss	Failures
Pure indirect inguinal.....	80%	10%	10%
Combined indirect and direct inguinal....	37%	50%	13%
Pure direct inguinal.....	30%	50%	20%
Recurrent postoperative inguinal.....	22%	50%	28%

100 dispensary visits. For these reasons it is not practical from an economic standpoint to recommend this method in compensation cases.

Considerable discussion and confusion exist as to certain salient points in the technic of the treatment. The importance of the chemical solution used has been overemphasized, largely because of commercial advertising. It has been our experience that many excellent,

12. Harris, F. I., and White, A. S.: Length of the Inguinal Ligament, J. A. M. A. 109: 1900 (Dec. 4) 1937.

properly prepared solutions are commercially available. In general they may be divided into two classes, those containing tannic acid in alcohol and those containing a fatty acid base. Experimental and clinical investigations have shown little difference in the fibrosis produced by the two types.<sup>13</sup> The fatty acid solutions have the practical advantage of a somewhat more simple

and is usually sufficient to satisfy a patient who has had two or three operative experiences.

If the object of the treatment is to offer the patient a possible cure or improvement with continued truss wearing, the field of usefulness of the injection method can be considerably extended. Many patients have hernias that produce symptoms but are denied operation because of their poor general condition. The injection method should be welcomed by surgeons as a valuable means of treating such patients.

Our experience has satisfied us that the prejudices against the injection method have been founded on theoretical misconceptions. On the other hand, the unwarranted enthusiasm for the method has been founded on reports of surgeons who have used the procedure but have failed to follow up critically their end results. The statistics presented in this paper offer an appraisal of the possibilities of the treatment of hernia by injection.

SUMMARY AND CONCLUSIONS

To evaluate the injection treatment in a study of 573 cases of hernia of all types, only 41 per cent, or 236 cases, could be utilized.

No serious complications or deaths occurred.

The 236 patients treated by injection have been followed up for from six months to three years after the completion of treatment. There were 57 per cent of cures, 28 per cent of possible cures and 15 per cent of complete failures.

This method of treatment if the object is cure should be limited to a small group of patients with pure indirect inguinal hernia. This group consists of young persons with recent hernial development whose inguinal ligament measures about 13 cm.

Reducible umbilical hernia in children can also be cured by the injection method.

The field of usefulness of the injection method can be considerably extended if the object is possible cure with continued truss wearing.

Recurrent postoperative inguinal hernia should be given a trial treatment by the injection method.

TABLE 14.—Number of Office Visits per Patient

Office Visits per Patient		Length of Time of Active Treatment	
Number of Patients	Number of Office Visits	Number of Patients	Number of Months of Active Treatment Not Counting Follow-Up
7	6-10	180	1-6
125	10-20	36	6-12
66	20-30	12	12-18
38	30-102	8	18-40
236		236	
Average number of office visits, 23		Average length of time of active treatment, 5.1 months	

This method of treatment is not simple and necessitates detailed care over a considerable period.

The most important single factor in the technic is the selection and application of a truss.

In general, the end results of the treatment of hernia by injection are not comparable to those obtained by operation. These results, however, are sufficiently good to recommend this treatment when operation cannot be considered because of economic, personal or physical reasons.

450 Sutter Street—516 Sutter Street.

TABLE 13.—Possibilities of Treatment in Selected Cases of Good and of Poor Risks

Type of Hernia	Approximate Result in Cases of Good Risks	Approximate Result in Cases of Poor Risks
Pure indirect inguinal.....	87% cures — wearing truss 13% failures	53% cures 43% wearing truss 4% failures
Combined indirect and direct inguinal	79% cures 11% wearing truss 11% failures	26% cures 60% wearing truss 14% failures
Pure direct inguinal.....	58% cures 33% wearing truss 9% failures	10% cures 62% wearing truss 29% failures
Recurrent postoperative inguinal	50% cures 41% wearing truss 9% failures	— cures 58% wearing truss 42% failures

application. The solutions used in the treatment of varicose veins are definitely dangerous and contraindicated in this technic.

Probably the most important single factor contributing to a successful result is the application of a scientifically correct truss. The importance of this far outweighs the value of any one solution over another. The selection and application of the truss necessitate accurate differential diagnosis of the type of inguinal hernia and require individual judgment for each patient. Probably the greatest obstacle to the popularization of this method lies in the general lack of knowledge on the part of surgeons of the principles of the construction and fitting of trusses.<sup>14</sup> It is our firm conviction that there can be no successful treatment of hernia by injection unless the patient is fitted with a proper truss.

Summing up our experience briefly, we believe that, if the object of treatment is cure, the injection method should be limited in its use to selected patients with pure indirect inguinal hernias. They should be young patients who are good risks, with recent hernial development, whose inguinal ligaments measure about 13 cm. Umbilical hernias in children offer an excellent field for this method. For persons who are good risks but whose inguinal hernia is of the combined indirect and direct type or the pure direct type, the results, while definitely not as favorable as those obtained with surgical methods, are sufficiently good to warrant recommendation of injection treatment when, for economic or personal reasons, operation is not possible. However, such patients should be made fully cognizant of the fact that the possibility of cure is less with the injection method than with operation. Recurrent postoperative inguinal hernias, which so often are the bane of the surgeon and the patient, are well worth treatment by this means. For, even if a cure is not obtained, improvement to the point of comfortable truss wearing can be promised

13. Harris, F. I.; White, A. S., and Biskind, G. R.: Observations on Solutions Used for Injection Treatment of Hernia, *Am. J. Surg.* 39: 112 (Jan.) 1938. Manoil, Lazarus: Histologic Effects of Various Sclerosing Solutions Used in the Injection Treatment of Hernia, *Arch. Surg.* 36: 171-189 (Feb.) 1938.  
14. Harris, F. I., and White, A. S.: The Truss in Relationship to the Diagnosis and Injection Treatment of Inguinal Hernia, *Am. J. Surg.* 36: 443 (May) 1937.

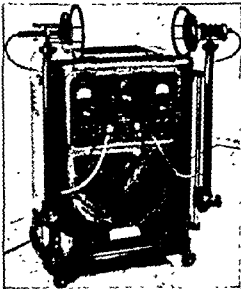
Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS.      HOWARD A. CARTER, Secretary.

SUPER FISCHERTHERM, MODEL 114-A-3  
ACCEPTABLE

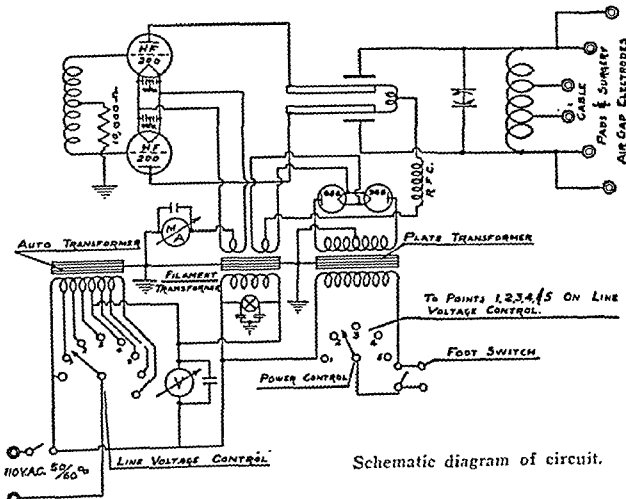
Manufacturer: The Fischer Corporation, 673 Ivy Street, Glendale, Calif.

The Super Fischertherm Short Wave Diathermy Unit, Model 114-A-3, is recommended for medical and surgical use in the office or hospital. This unit is similar to the Council accepted Super Fischertherm Unit, Model 114-A (THE JOURNAL, Dec. 18, 1937, p. 2064) except for the addition of higher powered tubes with necessary wiring changes and increased output, according to the firm. The cabinet housing is the same for the two units. Standard equipment includes inductance cable, cuff and pad electrodes and surgical accessories for coagulation, desiccation and cutting purposes. Air spaced electrodes and supporting arms are optional. No evidence was submitted concerning the ability of the unit to supply deep heat with air-spaced technic.



Super Fischertherm 114-A-3.

The circuit consists of two vacuum power tubes and two rectifier tubes in a simple arrangement. The output circuit is tuned by a split stator condenser. In adjusting for line voltage, an ohmite tap switch and a variable condenser resonance control are used. The newer model, 114-A-3, employs HF-300 Amperex tubes instead of HF-200 tubes. This change in tubes makes it necessary to use one more turn in the tank coil and slight change in filament voltage; i. e., 12 volts now delivered by filament transformer.



Schematic diagram of circuit.

The firm submitted the following physical data: When the machine was operated continuously for two hours at full load, the power input was approximately 1,990 watts. The average high frequency power output was 762 watts as measured by the calorimeter method. No part of the machine was unduly hot after the two hour run.

These data were later substantiated by tests made for the Council. The transformer temperature rise and the rise at various levels within the cabinet were within the limits of safety prescribed by the Council. The final temperature of the transformer when operating on lamp load of 520 watts was 79 C. The input was 1,540 watts. Burns may occur with this unit as with other short wave units but are less likely to occur than with conventional diathermy. A filter to inhibit feed-back of radio frequency current into the power line is included in the equipment.

In order to substantiate heating claims made for the unit, the firm submitted tests performed at a reliable laboratory. Four healthy male medical students served as subjects for these tests. Eight experiments each were performed with the inductance cable, cuff and pad technics. Temperature measurements were made with the thermocouple in the anterior portion of the thigh at depths of one-eighth, three-fourths and 2 inches or on the bone. These depths were measured from the skin straight in; that is, normal to the surface of the skin. The technic employed in the measurements was that recommended by the Council on Physical Therapy.

In applying the inductance cable approximately 1½ inches of bath toweling was wrapped around the thigh and held in place

Average of Eight Observations

Deep Muscle		Subcutaneous		Skin		Oral	
Initial	Final	Initial	Coil Final	Technic Initial	Final	Initial	Final
98.5	106.9	97.1	105.6	93.9	101.7	98.4	99.5
97.9 106.0		95.9 106.5		93.5 102.7		98.2 99.4	
98.4 104.1		97.2 102.3		93.9 99.7		98.4 99.1	

by approximately four wraps of the inductive cable. The averages for eight observations with this technic are given in the accompanying tables.

These data were accepted by the Council. The unit was investigated clinically for the Council and reported to function satisfactorily.

In the advertising copy submitted, the output is stated to be 762 watts as measured by the calorimeter method. That the physician may compare this value with the value obtained by the commonly used method, the Council lamp load output of 520 watts is also given.

In view of the foregoing report, the Council on Physical Therapy voted to accept the Super Fischertherm, Model 114-A-3, for inclusion in its list of accepted devices.

O. E. M. FACE TENT WITH  
OXY-ATOR ACCEPTABLE

Manufacturer: Oxygen Equipment Manufacturing Company, Inc., 247 East Fifty-Sixth Street, New York.

The O. E. M. Face Tent is recommended for intermittent oxygen therapy administered to conscious and cooperative patients. It is a boxlike mask, made of transparent plastacele (cellulose acetate) which forms a projection over the patient's nose, mouth and chin and is open at the bottom. It may be fitted to any adult face by molding the pliant aluminum framework. This is wrapped in moleskin. Malleable aluminum ear pieces, with loops at the ends, hold it in place. Tapes that tie back of the head may be used for the same purpose.



O. E. M. Face Tent with Oxy-Ator

In conjunction with the face mask, an Oxy-Ator is supplied to increase the efficiency of the equipment. This device attaches directly to the regulator. As oxygen is administered (in any flow from 6 to 12 liters per minute) the Oxy-Ator draws air into the circuit from the outside atmosphere, forming an air-oxygen mixture.

Oxygen is supplied by means of this rubber tubing, perforated on the portion inside the mask to direct the flow upward toward the center of the nostril. During expiration, oxygen collects in the mask and is forced out through the opening at the bottom. It is dry when admitted, since it has not passed through the water bottle. However, the firm claims that enough moisture from the exhaled air remains in the mask to provide a certain amount

of humidity. According to the firm, there is an almost immediate build-up of oxygen concentration in the face tent. The firm believes that additional cooling is not necessary if a continuous flow of 4 or more liters of oxygen is employed.

The unit was investigated clinically in the following manner:

The face tent and Oxy-Ator were used as directed and certain oxygen concentrations were obtained. The samples taken from patients and normal subjects were obtained with a small catheter from the oral pharynx at the end of forced expiration. The presence of carbon dioxide concentration approaching 4 to

*Analyses of Oxygen-Air Mixtures from Tube  
Connected to Oxy-Ator*

Rate of Oxygen Flow on Gage	Oxygen	Increased Rate of Flow Due to Air Added Through Oxy-Ator
4 liters oxygen per minute.....	92%	4.4 liters per minute
6 liters oxygen per minute.....	87%	7.1 liters per minute
8 liters oxygen per minute.....	86%	9.6 liters per minute

5 per cent is an indication that one has a sample of alveolar air. Of course, the oxygen percentages in this case are approximately 4 per cent less than the concentration that enters the lungs. This carbon dioxide determination has nothing to do with rebreathing of carbon dioxide from the mask. These analyses were determined on samples taken with the Oxy-Ator set to pick up the maximum amount of air.

CASE 1.—Normal healthy adult male with mask carefully fitted to face, subject sitting:

Oxygen Flow	Oxygen	Carbon Dioxide
4 liters per minute.....	25.6%	4.6%
6 liters per minute.....	33.0%	4.8%
8 liters per minute.....	48.8%	4.8%

The mask on the same subject was readjusted and the delivery tube changed so that it directed gas onto the upper lip in front of the nose:

Oxygen Flow	Oxygen	Carbon Dioxide
4 liters per minute.....	37.6%	4.8%
6 liters per minute.....	47.2%	4.8%
8 liters per minute.....	54.4%	4.6%

Comments: With a flow of 6 liters per minute, the mask was comfortable for a period of two hours. There was some tendency toward drying of the nasal mucous membranes. There was no clinical evidence of accumulated carbon dioxide as judged by observation of breathing. Analysis for carbon dioxide of samples taken during inspiration showed carbon dioxide from 0.2 to 0.4 per cent.

CASE 2.—Woman with hypertensive heart disease, decompensated, using the face tent and Oxy-Ator:

Oxygen Flow	Oxygen	Carbon Dioxide
6 liters per minute.....	68.8%	3.4%
8 liters per minute.....	76.0%	3.2%

These analyses were checked twice. This was the highest oxygen concentration obtained at any time.

CASE 3.—Patient dyspneic from pulmonary infarct and cardiac failure:

Oxygen Flow	Oxygen	Carbon Dioxide
6 liters per minute.....	43.8%	3.8%
8 liters per minute.....	58.0%	4.0%

This patient complained of the mask being too warm. Eight liters per minute was required to give him any relief.

This mask is useful, in the opinion of the Council, for the intermittent type of oxygen therapy. It can be kept on the face if the patient is quiet, conscious and cooperative. When properly

fitted to the face, it delivers a high concentration of oxygen in most cases but is variable in efficiency depending on the type of breathing and how it is applied to the face. The use of a device such as the Oxy-Ator appears to increase the efficiency of the face mask. However, a 6 liter flow of the air-oxygen mixture is necessary to eliminate the accumulation of carbon dioxide in the mask when used with Oxy-Ator. The hazard of very high oxygen concentration used over long periods of time must not be overlooked.

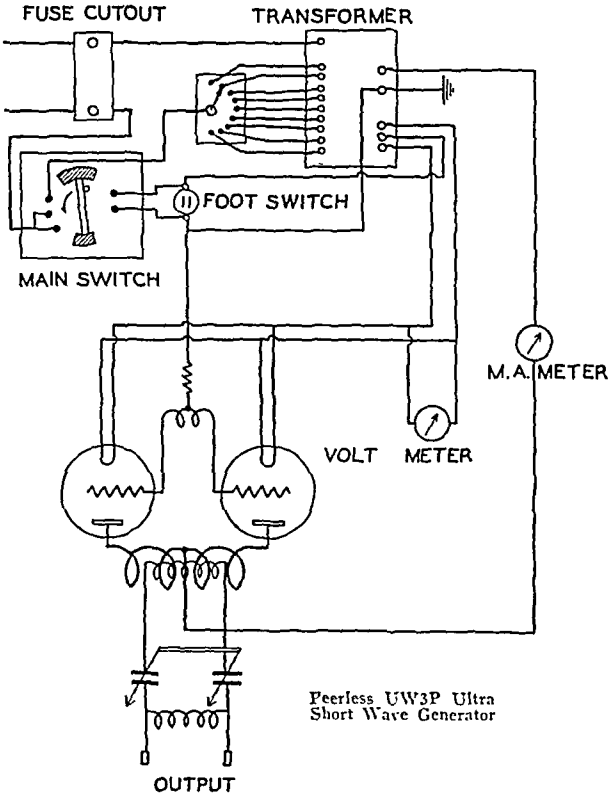
In view of the foregoing report, the Council on Physical Therapy voted to accept the O. E. M. Face Tent and the Oxy-Ator for inclusion in its list of accepted devices.

**PEERLESS ULTRA SHORT WAVE UNIT,  
MODEL UW3P, ACCEPTABLE**

Manufacturer: Peerless Laboratories, Inc., 115 East Twenty-Third Street, New York.

The Peerless Ultra Short Wave Unit, Model UW3P, is recommended for medical and surgical use. Pads, cuffs, inductance coil, treatment arms for air-spaced electrodes and metal electrodes are part of the standard equipment. Surgical accessories for cutting, desiccation and coagulation are available on request. The shipping weight of the machine is approximately 105 pounds.

Operating at a wavelength of 6 meters, it employs a two tube push-pull oscillating circuit. One branch of the patient's circuit



is inductively coupled and the other is capacitatively coupled to the oscillating circuit. The two branches of the patient's circuit are tuned simultaneously by means of a double condenser with parallel plates. A switching arrangement incorporated in the machine provides correct operating voltages to filament, plates and grids regardless of line voltage variations within a range of from 105 to 135 volts in a parallel line.

The unit has an input of approximately 700 watts. The output, as measured by lamp load, photoelectric cell and wattmeter, is approximately 325 watts. Temperature rise of the transformer and at various levels within the cabinet when operated at full load for approximately two hours was within the limits



prescribed for safety. The unit is licensed by the Electrical Research Products Corporation. Filters are to be included to prevent radio interference.

In addition, evidence was submitted by the firm to substantiate claims made for the heating ability of the unit when applied to the living human thigh. A reliable investigator performed tests with air-spaced electrodes. The technical procedure for making the tests was that recommended by the Council on Physical Therapy. Air-spaced circular electrodes, with average diameter

*Average of Six Observations, Air-Spaced Technic*

Deep Muscle Temperature		Oral Temperature	
Initial	Final	Initial	Final
99.1	104.7	98.7	98.9

of 4½ inches, were placed approximately 1¾ inches from the skin and 10 inches apart center to center. Six observations on the air-spaced technic only were given consideration and the averages are shown in the accompanying table.

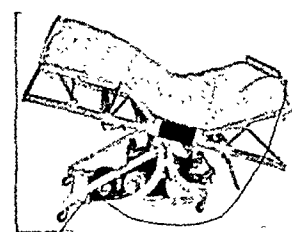
The apparatus was subjected to clinical study by a reliable investigator, who tried it with air-spaced electrodes and reported that it gave satisfactory service.

In view of the foregoing report, the Council on Physical Therapy voted to accept the Peerless Ultra Short Wave Unit, Model UW3P, for inclusion in its list of accepted apparatus.

### SANDERS VASOCILLATOR ACCEPTABLE

Manufacturer: American Hospital Supply Corporation, 1086 Merchandise Mart, Chicago.

The Sanders Vasocillator or Sanders Bed (as it was formerly called) is designed to aid circulation in peripheral vascular diseases by changing the posture of the patient at regular intervals. In appearance, the Vasocillator looks like an ordinary bed, consisting of an iron frame with coil springs supporting a felt mattress. The frame is mounted on a cradle and is geared to operate through an arc adjustable from 10 to 24 inch swings



*Sanders Vasocillator.*

(as measured at the head of the bed in relation to the floor) so that each end of the bed may be alternately high, in midposition or low. If desired, the bed may be held stationary at any desired angle. The oscillating mechanism, powered by a quiet motor, may be regulated according to the prescription of the physician. Its period of oscillation can be adjusted to take from one to seven minutes for a complete

cycle. The physician, the nurse or the patient may regulate the time to complete each cycle at will. The patient may lie flat or with the knees and feet elevated in relation to the body.

The Vasocillator is recommended by the firm for the treatment of peripheral vascular diseases such as threatened gangrene of diabetic or arteriosclerotic origin and of thrombo-angiitis obliterans without extreme capillary stasis (Buerger's disease).

Investigated in a clinic acceptable to the Council, the bed appeared to be a useful adjunct in the treatment of a limited number of peripheral vascular diseases due to capillary stasis, particularly in giving exercises similar to Buerger's exercises to individuals unable to perform active movements. The patients learn to sleep in the bed, thus continuing the exercise over long periods including day and night.

In the opinion of the Council, this bed has a limited therapeutic usefulness and no more can be expected from it than can be achieved by the conventional Buerger exercises. The Council points out that this oscillating bed is indicated for use in conjunction with other methods of treatment.

In view of the foregoing report, the Council voted to accept the Sanders Vasocillator for inclusion in its list of accepted apparatus.

## Council on Pharmacy and Chemistry

### REPORT OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.  
PAUL NICHOLAS LEECH, Secretary.

### VI-VEX NOT ACCEPTABLE FOR N. N. R.

Vi-Vex, manufactured by the Vi-Vex Manufacturing Company, Washington, D. C., was presented to the Council for consideration, with the information that the product consisted of 2 grains of phenacetin, 5 grains salicin, and ¼ grain caffeine citrated. The product is claimed to be relief for colds, grip, headaches, sinus and neuralgia if used "as prescribed by your physician or by the directions."

Such a product is in conflict with the rules of the Council; it consists of an unoriginal and also irrational mixture of well known drugs whose actions are also well known; the proprietary name is unwarranted and gives no information as to the composition of the product.

Vi-Vex is not a relief for all cases of colds, grip, headaches, sinus infection and neuralgia, and the advice on the label that if the case has progressed "take one every four hours" is an invitation to indiscriminate self medication. There is no reason why acetophenetidin should be combined with salicin (a salicyl preparation) in fixed proportions. If a physician desires to give an antipyretic combined with citrated caffeine it is his duty to prescribe it in the proportion indicated by the individual case.

The Council declared Vi-Vex unacceptable for inclusion in New and Nonofficial Remedies because it is an unscientific mixture sold with unwarranted and unestablished claims under an objectionable proprietary name.

### NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

**PROTAMINE ZINC INSULIN** (See New and Nonofficial Remedies, 1938, p. 338).

**Protamine, Zinc and Iletin (Insulin, Lilly)** (See New and Nonofficial Remedies, 1938, p. 338).

The following dosage form has been accepted:

*Protamine, Zinc & Iletin (Insulin, Lilly), 80 units, 10 cc.: Each cubic centimeter contains 80 units of insulin, together with protamine and approximately 0.16 mg. of zinc.*

**Protamine Zinc Insulin-Mulford** (See New and Nonofficial Remedies, 1938, p. 338).

The following dosage form has been accepted:

*Protamine Zinc Insulin-Mulford, 80 units, 10 cc.: Each cubic centimeter contains 80 units of insulin, together with protamine and approximately 0.16 mg. of zinc.*

**Protamine Zinc Insulin-Squibb** (See New and Nonofficial Remedies, 1938, p. 339).

The following dosage form has been accepted:

*Protamine Zinc Insulin-Squibb, 80 units, 10 cc.: Each cubic centimeter contains 80 units of insulin, together with protamine and approximately 0.16 mg. of zinc.*

**STAPHYLOCOCCUS TOXOID** (See New and Nonofficial Remedies, 1938, p. 422).

The National Drug Co., Philadelphia.

*Staphylococcus Toxoid (The National Drug Co.).—Prepared from toxin produced by selected strains of Staphylococcus aureus. The toxin, to which formaldehyde is added, is kept at 37 C. during the period necessary for the toxin to be converted into toxoid. The toxin is injected intradermally into rabbits to determine the smallest dose which will cause necrosis of the skin. After detoxification it must not produce necrosis in a dose of 0.2 cc. The toxin is tested for its hemolyzing action on rabbit cells; it must have a hemolytic test (L. H.) dose of not completely less. The detoxified toxin (toxoid) in a 1 cc. dose must not completely hemolyze a 1 per cent suspension of washed rabbit cells. Mice given intraperitoneal injections of 0.5 cc. doses of undiluted toxoid must survive four days; guinea pigs receiving 5 cc. of undiluted toxoid subcutaneously must have no local or general adverse symptoms during the period of observation (one week); rabbits receiving 3 cc. of toxoid per kilogram of*

weight, intravenously, must show no toxic symptoms within four days. Sterility tests are made by culture of toxoid in Smith fermentation tubes. The formaldehyde solution must not exceed 0.4 per cent by volume, 1 cc., 2 cc. and 3 cc. Potency tests are made in accordance with the requirements of the National Institute of Health: three doses of staphylococcus toxoid given, to rabbits intramuscularly at weekly intervals must produce at least 3 units of staphylococcus antitoxin per cubic centimeter of rabbit serum, as measured by the hemolytic method.

Staphylococcus toxoid (The National Drug Co.) is marketed in two dilutions: Dilution No. 1, 5 cc. ampul-vial containing in each cubic centimeter the equivalent of 100 minimum necrotizing doses of the original toxin; and Dilution No. 2, 5 cc. ampul-vial containing in each cubic centimeter the equivalent of 1,000 minimum necrotizing doses of the original toxin.

**CEVITAMIC ACID** (See New and Nonofficial Remedies, 1938, p. 480).

The following dosage form and brand have been accepted:

*Mead's Cevitamic Acid Tablets:* Each tablet contains 25 mg. cevitic acid equivalent to 500 international units of vitamin C.  
Prepared by Mead Johnson and Co., Evansville, Ind.

**Cebione** (See New and Nonofficial Remedies, 1938, p. 481).  
The following dosage forms have been accepted:

*Scaled Tubes Cebione, 0.5 Gm.*  
*Scaled Tubes Cebione, 1.0 Gm.*

**DIGITALIS** (See New and Nonofficial Remedies, 1938, p. 186).

*Capsules Digitalis Leaf, 0.1 Gm. (1½ grains)-Abbott:* Each capsule represents 1 U. S. P. unit.  
Prepared by Abbott Laboratories, North Chicago, Illinois.

**ANTIANTHRAX SERUM** (See New and Nonofficial Remedies, 1938, p. 394).

Jensen-Salsbery Laboratories, Inc., Kansas City, Mo.

*Antianthrax Serum.*—Prepared from cattle subjected to intradermal, followed by increasing doses of intravenous, injections of live cultures of *Bacillus anthracis*. Contains 0.5 per cent phenol as preservative. Marketed in vials containing 100 cc.  
*Dosage.*—Initial doses of from 50 to 100 cc. may be administered intravenously at three to twelve hour intervals as indicated; for subcutaneous injection, from 3 to 12 cc. into tissues about local lesions.

**EPHEDRINE HYDROCHLORIDE** (See New and Nonofficial Remedies, 1938, p. 227).

**EPHEDRINE HYDROCHLORIDE-LAKESIDE.**—A brand of ephedrine hydrochloride-U. S. P.

Manufactured by the Lakeside Laboratories, Inc., Milwaukee, Wis. No U. S. patent or trademark.  
*Solution Ephedrine Hydrochloride-Lakeside, 3%:* It is preserved with chlorbutanol, 0.5 per cent.

**EPHEDRINE SULFATE** (See New and Nonofficial Remedies, 1938, p. 228).

**EPHEDRINE SULFATE-LAKESIDE.**—A brand of ephedrine sulfate-U. S. P.

Manufactured by the Lakeside Laboratories, Inc., Milwaukee, Wis. No U. S. patent or trademark.  
*Ampoules Ephedrine Sulfate-Lakeside, 0.05 Gm. (¾ grain), 1 cc.*  
*Capsules Ephedrine Sulfate-Lakeside, 0.025 Gm. (¾ grain).*  
*Capsules Ephedrine Sulfate-Lakeside, 0.05 Gm. (¾ grain).*

**STRONG PROTEIN SILVER** (See New and Nonofficial Remedies, 1938, p. 443).

**SILVER PROTEIN STRONG-MERCK.**—A brand of strong protein silver-U. S. P.

Manufactured by Merck & Co., Rahway, N. J. No U. S. patent or trademark.

**ETHYL AMINO BENZOATE** (See New and Nonofficial Remedies, 1938, p. 80).

**BENZOCAINE-MERCK.**—A brand of ethyl aminobenzoate-U. S. P.

Manufactured by Merck & Co., Rahway, N. J. No U. S. patent or trademark.

**BISMUTH AND POTASSIUM TARTRATE** (See New and Nonofficial Remedies, 1938, p. 146).

**BISMUTH AND POTASSIUM TARTRATE-MERCK.**—A brand of bismuth and potassium tartrate-U. S. P.

Manufactured by Merck & Co., Rahway, N. J. No U. S. patent or trademark.

**CARBROMAL** (See New and Nonofficial Remedies, 1938, p. 155).

**CARBROMAL-MERCK.**—A brand of carbromal-U. S. P.

Manufactured by Merck & Co., Rahway, N. J. No U. S. patent or trademark.

## Council on Foods

### ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION AND WILL BE LISTED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED.

FRANKLIN C. BING, Secretary.

#### LARSEN'S "FRESHLIKE" BRAND STRAINED VEGETABLE SOUP

*Manufacturer.*—The Larsen Company, Green Bay, Wis.

*Description.*—Canned, strained vegetable soup containing carrots, potatoes, barley, tomatoes, peas, green beans, celery, spinach and salt.

*Manufacture.*—Selected fresh vegetables are cleaned, trimmed, peeled, mixed with whole barley grains and salt, vacuumized, cooked to proper softness and texture, and double screened. The mixture is filled into cans, sealed under vacuum, and heat processed.

*Analysis* (submitted by manufacturer).—Moisture 85.3%, total solids 14.7%, ash 1.1%, fat (ether extract) 0.2%, protein (N × 6.25) 2.2%, crude fiber 0.5%, carbohydrates other than crude fiber (by difference) 10.7%, calcium (Ca) 0.027%, phosphorus (P) 0.157%, iron (Fe) 0.0009%.

*Calories.*—0.5 per gram; 14 per ounce.

#### CLAPP'S CHOPPED APPLE SAUCE

*Manufacturer.*—Harold H. Clapp, Incorporated, Rochester, N. Y.

*Description.*—Canned apple sauce prepared from chopped apples, sweetened with sugar.

*Manufacture.*—Baldwin apples are graded, washed to remove spray residues, again washed, peeled, cored, inspected, trimmed by hand, water sprayed and mechanically chopped. The apples are weighed and a definite amount of sugar is added. The mixture is heated in an atmosphere of steam, adjusted to standard consistency, filled into cans, sealed, processed under pressure in steam retorts and cooled.

*Analysis* (submitted by manufacturer).—Moisture 85.8%, total solids 14.2%, ash 0.4%, fat (ether extract) 0.7%, protein (N × 6.25) 0.1%, crude fiber 2.1%, carbohydrates other than crude fiber (by difference) 10.9%.

*Calories.*—0.5 per gram; 14 per ounce.

#### MRS. PALEY'S BABY FOOD—STRAINED BEEF

*Manufacturer.*—Paley-Sachs Food Company, Houston, Texas.

*Description.*—Canned sieved scraped beef, U. S. inspected and passed by the Department of Agriculture. Slightly seasoned with salt.

*Manufacture.*—Lean beef, U. S. inspected and passed by the Department of Agriculture, is scraped to remove tough sinew, and ground. Definite proportions of water and salt are added and the mixture is heated to from 71 to 77 C., strained, filled into cans, sealed and heat processed at 116 C. for one hour.

*Analysis* (submitted by manufacturer).—Moisture 82.5%, total solids 17.5%, ash 1.6%, fat (ether extract) 0.5%, protein (N × 6.25) 14.4%, carbohydrates (by difference) 1.0%.

*Calories.*—0.66 per gram; 19 per ounce.

#### CELLU BRAND TOMATO JUICE

*Distributor.*—Chicago Dietetic Supply House, Inc., Chicago.

*Description.*—Canned tomato juice; no added salt.

*Manufacture.*—Manufactured in essentially the same manner as Kemp's Sun-Ray Brand Tomato Juice (THE JOURNAL, Dec. 13, 1930, p. 1835).

*Analysis* (submitted by manufacturer).—Moisture 94.4%, total solids 5.6%, ash 0.4%, fat (ether extract) 0.3%, protein (N × 6.25) 1.0%, reducing sugar as invert 3.6%, sucrose (by copper reduction) 0.1%, crude fiber 0.2%, carbohydrates other than crude fiber (by difference) 3.7%.

*Calories.*—0.22 per gram; 6 per ounce.

# THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, NOVEMBER 26, 1938

## ASPHYXIA OF THE NEWBORN

According to the statistics of the birth registration area about 80,000 infants die annually at birth in this country; 30,000 more die on the first day from causes which, almost without exception, are of natal origin. For every hundred babies born alive there are five, or one in twenty, that die within the first twenty-four hours of extra-uterine life. As Yandell Henderson pointed out, the first quarter of an hour after birth is the most dangerous period of life. Its mortality is as great as that of any subsequent month. The principal causes of infant mortality during the first twenty-four hours are prematurity, cerebral hemorrhage and asphyxia. These factors are so interrelated that it is impossible to establish precisely their relative importance. Intra-uterine pneumonia due to aspiration of amniotic fluid, plus a bacterial factor, are responsible for a certain number of deaths and, rarely, drugs administered to the mother.

Apnea of the newborn naturally demands consideration of the mechanism which initiates the respiration shortly after the fetus is born and the cord is clamped. The mechanical theory of Preyer that the reflex stimulation of the trauma of labor acts as a stimulant to the respiratory center is contradicted by everyday clinical observations. Rough palpation, attempts at manual version or application of forceps do not initiate breathing as long as the fetus remains in utero with the placental circulation intact. The mechanical theory led to the establishment of the time honored and not infrequently vicious methods of resuscitation, such as slapping, swinging or plunging the infant into an ice cold bath. Ahlfeld delivered several women in a warm saline bath and found that respiration began as usual, thus refuting the view that skin irritation as the result of exposure to air and change of temperature causes the infant to breathe. The chemical theories advanced in explanation of the initiation of the first gasp after the cord is clamped were (1) insufficient oxygen, (2) excess of carbon dioxide and (3) increased blood

pressure in the brain. Barcroft<sup>1</sup> administered a carbon dioxide mixture to the mother and noted that it had no effect whatever on the infant. Eastman<sup>2</sup> studied the carbon dioxide tension of the blood in infants at birth and found that respiration began whether the tension of this gas was high or low and seemed to bear no relationship to the carbon dioxide tension. Barcroft established in the goat that lack of oxygen is the cause of the onset of respiration. According to Eastman's investigations, however, the oxygen content of the blood at birth showed no relationship between the concentration of this gas and respiration except possibly that infants with a high content of oxygen in the blood breathe more readily and that those with an extremely low content are apneic.

An entirely different approach to the problem was made possible by the unique investigations of Snyder and Rosenfeld.<sup>3</sup> They have established the existence of rhythmic respiratory movements of the fetus in utero long before term. Their method consisted of sectioning the spinal cord of the maternal animal at the level of the second lumbar vertebra, under local anesthesia, in order to permit laparotomy without the use of a general anesthetic. Incision of the abdomen at the lower midline was carried out beneath the surface of a bath of Ringer solution at 37 C. The gravid uterus readily escaped from the peritoneal cavity and came under direct observation. Gases and volatile anesthetics were administered through a T shaped cannula introduced by tracheotomy under local anesthesia. The authors have observed the occurrence of regular respiratory movements under these experimental conditions in full term fetuses. They have thus established that the fetal respiration is not initiated at birth and that the fetuses of the rabbit, cat and guinea pig show rhythmic respiratory movements within the uterus, instead of a state of prolonged apnea. They have further established that the regularity of fetal respiration depends on the oxygen and the carbon dioxide level of fetal blood, that the oxygen want depresses or abolishes fetal respiratory movements and that a carbon dioxide deficit results in depression or apnea of the fetus, showing that a certain level of carbon dioxide is essential for the maintenance of fetal respiration.

Snyder and Rosenfeld also made observations of the fetal movements transmitted through the abdominal wall in a series of women near term.<sup>4</sup> They recognized unmistakable, spontaneous fetal movements which continued at the regular rhythm for many minutes. These movements were recorded with the aid of motion pictures. They have thus given both experimental and

1. Barcroft, Joseph: Certain Changes in Circulation and Respiration Occurring at Birth, *J. Physiol. U. S. S. R.* 19:29, 1935.

2. Eastman, N. J.: Asphyxia Neonatorum, *Internat. Clin.* 2:274 (June) 1936.

3. Snyder, F. F., and Rosenfeld, Morris: Direct Observation of Intra-Uterine Respiratory Movements of the Fetus and the Role of CO<sub>2</sub> and Oxygen in Their Regulation, *Am. J. Physiol.* 119:153 (May) 1937.

4. Snyder, F. F., and Rosenfeld, Morris: Intra-Uterine Respiratory Movements of the Human Fetus, *J. A. M. A.* 108:1946 (June 5) 1937.

clinical confirmation of the intra-uterine respiratory activity first advanced by Schultze, Ahlfeld, Weber and Reifferscheid. In view of these facts the respiratory failure of the newborn must be regarded, according to Snyder and Rosenfeld, as an expression of a previous activity suppressed rather than failure of some new mechanism to begin functioning at birth.

The keynote to the treatment of asphyxia neonatorum, as emphasized by Eastman in his illuminating review, is gentleness. The removal of fluid and mucus from the air passages is the first step and in most instances the only one required. This may be accomplished by posture, by gentle wiping of the mouth and pharynx with the little finger covered by gauze, and by the use of suction with a catheter. The simplest, as well as the oldest, method of mouth to mouth insufflation has its obvious practical advantages as well as definite limitations and objections, the principle of which is that rupture of the pulmonary alveoli may occur unless the method is practiced gently.

Yandell Henderson warns obstetricians to be more conservative in administering narcotics shortly before delivery,<sup>5</sup> in view of the ample evidence that such drugs act far more on the baby than on the mother. He further emphasizes that the passage of a soft catheter into the trachea of an apneic baby is so simple an operation and insufflation by the Meltzer-Flagg technic is so effective that there is little justification for any other procedure. The technic for artificial respiration of the newborn presented by Flagg<sup>6</sup> insists on adherence to surgical principles, namely exposure of the field with the aid of a small laryngoscope, removal of foreign material under direct vision and, when necessary, endotracheal intubation and insufflation of oxygen and carbon dioxide under controlled pressure.

### PROTRACTED MODERATE SCURVY

Szent-Györgyi,<sup>1</sup> who has contributed much of our accurate knowledge of the nature of vitamin C and the body's requirements for this substance, has reiterated his opinion that the quantity of vitamin C which protects the organism against scurvy may not be sufficient for optimal health and growth, because scurvy is not the first sign of vitamin C deficiency but rather a late, if not actually premortal, symptom. Man, it is said, lives under conditions in our present civilization which subject him frequently to partial vitamin deficiency. Such deficiencies may fail to produce definite characteristic symptoms but if continued for a sufficient time will bring about pathologic changes. The clinical symptoms which result from protracted or intermittent suboptimal intake of vitamin C have been too indefinite

to constitute acceptable criteria for establishing the diagnosis of chronic vitamin C deficiency.

Accurate visualization of the pathologic changes in the bones and cartilage which may result from a protracted mild deficiency of vitamin C for children and for adults has been accomplished by Park, Guild, Jackson and Bond,<sup>2</sup> by Wolbach and Howe<sup>3</sup> and more recently by Ham and Elliott.<sup>4</sup> Various workers have expressed differences of opinion or of interpretation of the pathologic changes. Park and his associates included a thorough analysis of the roentgenologic appearance as well as microscopic changes in the scorbutic bones of children. They believe that bones continue to grow in length in scurvy because the cartilaginous epiphysal plate continues to grow. They think, however, that the cartilage is piled up unossified on the diaphysal side of the plate as a honeycomb of heavily calcified cartilage which shows readily in the roentgenograms.

Ham and Elliott used guinea pigs of both sexes fed on a diet which contained less than the basic requirement of vitamin C but a sufficient amount of this vitamin to prevent the development of the more commonly recognized results of acute scurvy. The control animals received, in addition to the basal diet, 1 cc. of orange juice per hundred grams of body weight, plus an additional 1 cc. as a margin of safety, in accordance with the recommendation of Dann and Cowgill.<sup>5</sup> Observations were made on five groups of animals: controls, those receiving no vitamin C, and three groups, each of which were subjected to a different degree of deficiency. Since the diaphysal lesions of severe scurvy had already been carefully studied in both man and the experimental animals by several investigators, the results in this group were not included. In the experimental animals the epiphysal plate was thinner than in the normal animals and there was not the accumulation of cartilage on the diaphysal side of the plate which had been described by Park and his associates and which, in all probability, represented a much more acute phase of this deficiency disease.

In protracted moderate scurvy, which probably approximates that most commonly seen in human beings, the experimental animals showed microscopic changes both in the diaphyses and in the epiphyses. The cancellous scaffolding of bony trabeculae in the juxta-epiphysal region of the diaphysis was poorly formed. The number and activity of the cells concerned in building this bony scaffolding was diminished. Although growth of the bones continued, they became exceedingly weak and fractures were commonly found

5. Henderson, Yandell: *Resuscitation*, J. A. M. A. **109**: 1561, (Nov. 6) 1937.

6. Flagg, P. J.: *Asphyxia Neonatorum*, Surg., Gynec. & Obst. **67**: 153 (Aug.) 1938.

1. Szent-Györgyi, Albert: *Therapeutic Properties of Vitamins*, Presse méd. **46**: 995 (June 22) 1938.

2. Park, Edward A.; Guild, Harriet G.; Jackson, Deborah, and Bond, Marian: *The Recognition of Scurvy with Especial Reference to the Early X-Ray Changes*, Arch. Dis. Child. **10**: 265 (Aug.) 1935.

3. Wolbach, S. Burt, and Howe, Percy R.: *Intercellular Substances in Experimental Scorbute*, Arch. Path. & Lab. Med. **1**: 1 (Jan.) 1926.

4. Ham, A. W., and Elliott, H. C.: *The Bone and Cartilage Lesions of Protracted Moderate Scurvy*, Am. J. Path. **14**: 323 (May) 1938. Elliott, H. C.: *Studies on Articular Cartilage: I. Growth Mechanism*, Am. J. Anat. **58**: 127 (Jan.) 1936.

5. Dann, Margaret, and Cowgill, George R.: *The Vitamin C Requirement of the Guinea-Pig*, J. Nutrition **9**: 507 (April) 1935.

on the diaphysial side of the epiphysial plate. The epiphysial cartilage plate was thinner than in the control animals at the point where it caps the marrow cavity, and the columns of cartilage cells were less regular. The microscopic examination of the epiphyses revealed an uncalcified zone in the region nearest the articular cartilage and a calcified zone in the layer of bone which underlies and supports the articular cartilage. The supporting bone was diminished in amount and in some places there was none to support the articular cartilage itself. Ham and Elliott are convinced that in growing scorbutic bones the portion of the shaft laid down before the onset of the disease was affected much less than the tissue laid down afterward. This would indicate that scurvy inhibits the formation of new bone more than it speeds up bone absorption.

The "jellation theory" was advanced by Aschoff and Koch,<sup>6</sup> who observed that zones of active normal bone formation were replaced in scurvy by a marrow framework which contained little firm intercellular substance. In 1926 Wolbach and Howe studied the bones of scurvy and stated that they believed the loose texture described by Aschoff and Koch was caused by the presence of liquid intercellular substance. This liquid intercellular substance, according to this theory, simply failed to jell because it lacked the cement material. Ham and Elliott did not agree but reported that they found no evidence of the accumulation of a jelling fluid intercellular substance. On the contrary, there seemed to be a general depression of all the activity usually concerned in bone formation.

#### BONE MARROW IN APLASTIC ANEMIA

The exact nature of the cellular changes in the bone marrow in aplastic anemia has received little attention despite the fact that numerous clinical studies have been made on patients with this disease. Some evidence,<sup>1</sup> however, suggests that the abnormality is not necessarily a lack of immature forms of erythrocytes in the bone marrow, as hyperplasia of the marrow rather than aplasia is frequently found. It might be concluded, therefore, that in this type of anemia there is a failure of the normal process of maturation of the red cell. However, the fact should be emphasized that the abnormality in maturation of erythrocytes which occurs in aplastic anemia must differ from that in pernicious anemia, as liver therapy does not favorably affect the former.

The suggestion that there is an impairment in the maturation of erythrocytes in aplastic anemia has recently been investigated further<sup>2</sup> on patients with

this disease. Differential counts were made on biopsy specimens of sternal marrow stained both supravitaly and in the ordinary way. The pathologic changes in the cellular composition of the marrow permitted classification into five distinct groups. In one the characteristic feature was a replacement of hemopoietic tissue by a cellular structure composed of megakaryocytes in various stages of development, a true "myelophthisic anemia." In the second group the marrow was sclerotic and, in the remaining three groups, differences only in the cellularity of the marrow were evident. In the latter three the marrows were either aplastic, active or hyperplastic; in each, however, the fundamental abnormality was a failure of maturation of the hemopoietic cells at an early undifferentiated stage. This observation thus supports the view that a primary etiologic factor in aplastic anemia is an impairment in the normal process of erythrocyte maturation.

Another observation of particular interest was the similarity between the appearance of the marrow from patients with aplastic anemia and that from patients with acute agranulocytosis. A similar failure in the process of cell maturation was observed. The authors therefore suggest that "aplastic anemia and acute agranulocytosis may have some etiologic factor in common." In practical support of this view, it is pointed out that anemia frequently supervenes in cases of chronic agranulocytosis, in which early death or spontaneous remissions do not occur and thus mask the more slowly developing disturbances in erythropoiesis. This significant suggestion merits continued careful investigation.

#### Current Comment

##### TYPHOID MARY DIES

The death on November 11 of Mary Mallon, aged 70, who achieved notoriety as the first typhoid carrier recognized in the United States, brings to a close a strange history. "Typhoid Mary" was a cook whose employment was almost invariably accompanied by an outbreak of typhoid. Her role in the spread of this disease was finally recognized in 1907 and she was forcibly kept out of circulation at the Detention Hospital of the Health Department for three years. Following her voluntary release in 1910 she disappeared for five more years and, although her history neither before her first detention nor after her disappearance could be learned completely, she was known to have caused at least ten outbreaks of typhoid with fifty-one cases. From 1915 until her recent demise she was held by the New York City Department of Health in the Riverside Hospital on North Brother Island. She became reasonably adapted to her changed status, and her stools were constantly used by the health department as a control for mediums used in the culture of typhoid bacilli. "Typhoid Mary" will be known forever in association with the typhoid carrier problem.<sup>1</sup>

6. Aschoff, Karl Albert Ludwig, and Koch, W.: *Skorbut*, Jena, Gustav Fischer, 1919, pp. 56-84.

1. Sheard, Arthur: *A Contribution to the Study of Pernicious Anemia and Aplastic Anemia*, New York, William Wood & Co., 1924.

2. Thompson, W. P.; Richter, N. M., and Edsall, K. S.: *Analysis of So-Called Aplastic Anemia*, *Am. J. M. Sc.* 187:77 (Jan.) 1934.

2. Rhoads, C. P., and Miller, D. K.: *Histology of the Bone Marrow in Aplastic Anemia*, *Arch. Path.* 26:648 (Sept.) 1938.

1. Soper, George A.: *Typhoid Mary*, *Mil. Surgeon* 45:1 (July) 1919.

## Association News

### JUDGE LIMITS SCOPE OF GRAND JURY INVESTIGATION

District Court Justice Proctor on November 17 quashed two thirds of a subpoena which had ordered the American Medical Association to produce to the grand jury a wide variety of certain records, some going back as far as twenty-two years. In ordering the first two paragraphs of the subpoena quashed, Judge Proctor struck out that part which ordered the American Medical Association to produce certain records dealing with the following organizations: Illinois Social Hygiene League; Public Health Institute; United Medical Service; Civic Medical Center and Dr. Louis E. Schmidt, all of Chicago; Milwaukee Medical Center, Milwaukee; Trinity Hospital, Little Rock, Ark.; Ross-Loos Medical Group, Los Angeles, and Community Hospital, Elk City, Okla. The original subpoena had ordered a sweeping probe of all records concerning these organizations. In his opinion, Justice Proctor is reported to have said:

The assertions made in the motion and in arguments that compliance with the subpoena will require an examination for the stated period of every paper in all the files of the Association scattered through its separate departments, occupying a large nine-story building in Chicago, have not been challenged in any way. The statement seems to be fair when one visualizes the situation in the light of the sweeping terms of the subpoena. To fully and strictly comply therewith every paper of whatever nature containing the slightest reference to the ten named organizations and persons for the periods specified must be found and produced. In most cases the dates go back to 1930; in one case to 1916. In addition it would be necessary to find over a period of about four years all papers of every kind containing any possible reference to persons or bodies engaged in providing, proposing or attempting to provide prepaid medical care or low-cost group medical practice. The marks for identifying these papers are not prescribed subjects that might have some possible relevancy to the nature of the grand jury's investigation. The only means for finding them is to examine all papers for some reference, however casual or unimportant, to specify classes of persons, apparently large, who may in any way have been engaged in any movement to promote prepaid or low-cost group medical service. Moreover, it is presupposed that the Association knows the names of all those so engaged. Doubtless many are known, but it seems likely they would be met with great difficulty and uncertainty in attempting to identify all. In a few of these considerations, I cannot but regard the provisions of the first and second paragraphs of the subpoena as imposing an unreasonable and oppressive burden.

The third paragraph of the subpoena, which Justice Proctor allowed to stand, orders the American Medical Association to produce all correspondence, memoranda or other documents, dating from Jan. 1, 1932, relating to:

The Justice Department's investigations of relations of the American Medical Association and the District Medical Society with the Group Health Association Inc. of Washington, D. C.

Any requirement or proposal of the American Medical Association that hospital staff members belong to local branches of the American Medical Association.

Instances where approval of hospitals for intern training by the American Medical Association were revoked because of the membership of the staffs of such hospitals.

In his opinion, as noted, Justice Proctor considered the demand of the records indicated in the first two sections of the subpoena as "an unreasonable and oppressive burden."

### HEARINGS BEFORE THE GRAND JURY IN WASHINGTON

The following four witnesses from the Episcopal Eye, Ear and Throat Hospital, Washington, D. C., are reported to have appeared last week before the Special Grand Jury in Washington, D. C.: Henry P. Blair, chairman of the executive committee; Miss Anita Richardson, staff secretary; Dr. Carl Henning, secretary of the board of directors, and Dr. Maurice A. Selinger, secretary of the medical board. Dr. Thomas E. Mattingly, Washington, D. C., also testified before the grand jury.

### RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company, entitled "Your Health," began Wednesday October 19 and will run consecutively for thirty-

six weeks. The program is broadcast over the Blue network of the National Broadcasting Company each Wednesday at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).<sup>1</sup>

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

November 30. Rest, Relaxation and Recreation.  
December 7. Tuberculosis and the Teens.  
December 14. What Shall We Eat?

### EXHIBIT SYMPOSIUM ON HEART DISEASE

An exhibit symposium on heart disease has been arranged for the Scientific Exhibit at the St. Louis session of the American Medical Association, May 15-19, 1939. The symposium will be presented with the cooperation of the American Heart Association, under the auspices of a committee of which Dr. Thomas M. McMillan, 2044 Locust Street, Philadelphia, is chairman. Application blanks for space in the exhibit may be obtained from Dr. McMillan or from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago.

## Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ADDITIONAL MEDICAL COLLEGE NEWS AND ARTICLES APPEAR IN THE STUDENT SECTION, PAGE 2059.

### ARKANSAS

**Changes in Health Officers.**—Dr. Ulys Jackson, Harrison, has been appointed medical director of district 14 of the state department of health, with headquarters in Marshall.—Dr. Earnest L. Thompson, Hot Springs National Park, has been appointed in charge of the Gariand County health department, succeeding the late Dr. James F. Merritt.

**Society News.**—The White County Medical Society was addressed September 14 in Searcy by Drs. Doyle W. Fulmer on "Malaria in Arkansas"; Barnett P. Briggs, "Respiratory Infections in Children," and Merlin J. Kilbury, "Changes in the Cervix and Uterus." All are of Little Rock.—At a meeting of the Ouachita County Medical Society in Camden September 1 the speakers were Drs. Raymond C. Cook and Kingsley W. Cosgrove, both of Little Rock, on "External Diseases of the Eye of Interest to the General Practitioner" and "The Ophthalmoscope and the General Practitioner" respectively.—Dr. Frederick H. Krock, Fort Smith, discussed "Factors in Estimation of Disability" before the Sebastian County Medical Society September 13.

### CALIFORNIA

**Course on Fractures.**—The University of California Medical School, San Francisco, will offer a course on "Treatment of Fractures" at the San Francisco Hospital December 14-16. The course, which will be short and comprehensive, has been designed to meet the needs of physicians engaged in private practice. Additional information may be obtained from the dean's office at the university, Medical Center, San Francisco.

**Society News.**—Dr. Lodewyk Bendikson, Los Angeles, discussed "The Technical and Scientific Program of a Modern Research Library" before the Hollywood Academy of Medicine November 10.—The San Francisco County Medical Society devoted its meeting November 8 to a symposium on pneumonia

1. Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.



with the following speakers: Drs. Herbert C. Moffitt, Jacob C. Geiger, John W. Brown and Edwin L. Bruck, Miss Cordula Kohl and Miss N. M. Anderson, R.N.

### CONNECTICUT

**Parrots Barred from Connecticut.**—The importation of parrots into Connecticut is prohibited under a recent revision of the state sanitary code. The regulation also prohibits the purchase, breeding, sale or giving away of any birds belonging to the psittacine family but provides that the importation or breeding of such birds for scientific research or exhibition in public zoological gardens may be permitted subject to the approval of the state department of health.

**The Terry Lectures.**—Dr. Henry E. Sigerist, director of the Institute of the History of Medicine, Johns Hopkins University School of Medicine, Baltimore, delivered the Dwight Harrington Terry Foundation lectures at Yale University School of Medicine, New Haven, November 2-5. The main topic of discussion was "Medicine and Human Welfare"; individual titles of the lectures were "The Significance of Disease," "The Significance of Health" and "The Physician's Mission." The lectures are named after the late Dwight H. Terry, Plymouth, who gave \$100,000 to establish the lectureship.

### GEORGIA

**The Jonte Equen Memorial Lecture.**—Dr. Wells P. Eagleton, Newark, N. J., delivered the second Jonte Equen Memorial Lecture before the Fulton County Medical Society, Atlanta, October 21. His subject was "Allergic and Toxic Types of Curable Bacterial Meningitis." The lectureship was established a year ago by Dr. Murdock Equen in memory of his father.

**District Meeting.**—The Second District Medical Society was addressed in Bainbridge October 14, among others, by Drs. John W. Mobley Jr., Pelham, on "Hookworm—Its Economic and Medical Importance in Southwest Georgia"; Thomas C. Davison, Atlanta, "Thyroids," and Walter P. Rhyne, Albany, "Relationship of Nasal Infection and Sinusitis with Infection of the Middle Ear."

**Society News.**—Dr. Grayson L. Carroll, St. Louis, addressed the Georgia Urological Association in Atlanta October 13 on "The Trend Toward Conservatism in Urological Treatment."—The Fulton County Medical Society was addressed October 20 by Drs. Benjamin Russell Burke and William B. Armstrong on "The Normal and Pathologic Larynx" and by Drs. Earle H. Floyd and James L. Pittman on "The Recuperative Powers of the Kidney."

### ILLINOIS

**Conference of Health Officers and Public Health Nurses.**—The annual conference of Illinois Health Officers and Public Health Nurses will be held in the auditorium of the Centennial Building, Springfield, November 30-December 1, with Dr. Albert C. Baxter, acting state health director, as chairman. Out of state speakers will include:

- Dr. Wilson G. Smillie, New York, The Development of Public Health in the United States.
- Dr. Harry S. Mustard, New York, Rural Health Problems.
- Dr. Bruce Douglas, Detroit, Newer Aspects of the Tuberculosis Problem.
- Dr. Adolph S. Rumreich, U. S. Public Health Service, Washington, D. C., Administrative Control of Pneumonia.
- Dr. Nels A. Nelson, Boston, Administrative Control of Syphilis and Gonorrhea.
- Dr. Gaylord W. Anderson, Minneapolis, Scarlet Fever Control.
- Dr. Arthur T. McCormack, Louisville, Ky., Outlook in Public Health.
- Dr. Franklin G. Ebaugh, Denver, Mental Hygiene in Public Health.
- Sophie Nelson, R.N., Boston, Organizing Community Nursing Service.
- John C. Brauer, D.D.S., Des Moines, Dental Hygiene in Public Health.

### Chicago

**Annual Institute Meeting.**—Dr. Joseph A. Capps will deliver the presidential address at the twenty-third annual meeting and dinner of the Institute of Medicine of Chicago December 6; his subject will be "Prognosis of Subacute Bacterial Endocarditis."

### INDIANA

**Changes in Health Officers.**—Dr. William D. Hart has been appointed director of district health unit 4, Rising Sun, succeeding Dr. George M. Brother, who is taking a year's study at Johns Hopkins University School of Hygiene and Public Health, Baltimore. Dr. Lewis C. Robbins is acting chief of the bureau of local health administration, state board of health, Indianapolis, while Dr. John W. Ferree, chief of the bureau, completes a course at the school of hygiene and public

health.—Dr. John S. Woolery, Bedford, has been appointed health officer of Lawrence County, filling the unexpired term of the late Dr. Wesley H. McKnight.

**Society News.**—The Fayette-Franklin County Medical Society was addressed in Connersville October 11 by Dr. Don E. Kelly, Indianapolis, on "Treatment of Common Skin Diseases."—The Parke-Vermillion County Medical Society heard Dr. Caryle B. Bohner, Indianapolis, discuss "Diagnosis and Treatment of Allergic Diseases" October 19.—Dr. Florian E. Schmidt, Chicago, addressed the Montgomery County Medical Society in Crawfordsville October 20 on "Serum Treatment of Pneumonia."—At a meeting of the St. Joseph County Medical Society in South Bend October 18 the speakers were Drs. Fred P. Eastman and Edward L. Rigley, South Bend, on "History of Early Medicine in St. Joseph County" and "Intrinsic Lesions of the Esophagus."—Dr. John E. Dalton, Indianapolis, discussed "Syphilis and the Pregnant Woman" before the Randolph County Medical Society in Winchester October 10.—The Floyd County Medical Society was addressed in New Albany October 14 by Dr. James W. Baxter Jr., New Albany, on "Sulfanilamide and Estrogenic Substance."

### KANSAS

**Health Talks for School Children.**—The speakers' bureau of the Sedgwick County Medical Society began a series of lectures October 27 to continue for sixteen weeks designed for school boys on topics of general health interest. The list of subjects coincides with the topics to be broadcast for a given week on the American Medical Association's radio program "Your Health." The talks are twenty minutes in length followed by twenty minutes of discussion and will be given in the auditorium of the North and East high schools, Wichita, Mondays and Thursdays respectively.

**Society News.**—Dr. Fred J. McEwen, Wichita, addressed the Mitchell County Medical Society at Beloit October 12 on the electrocardiograph.—At a meeting of the Wichita League for the Hard of Hearing October 12 Drs. Lloyd Gilbert Little spoke on "The Psychiatric Aspect of the Hard of Hearing" and Ernest E. Tippin, "Conservation of Hearing."—The Johnson County Medical Society was addressed in Olathe October 10 by Drs. Wayne C. Bartlett and James S. Hilbard Jr. on "Surgical Gallbladder" and "Surgical Treatment of Ulcerous Lesions of the Stomach" respectively.—At a meeting of the Pratt County Medical Society October 28 Drs. Christian A. Hellwig spoke on "Uterine Bleeding After the Age of Forty" and Howard C. Clark, "Prenatal Care." Both are from Wichita.—The Wyandotte County Medical Society was addressed October 18 by Drs. Ingall H. Neas, Kansas City, on "Pneumothorax Therapy" and Leland F. Glaser, Kansas City, "Clinical Results Obtained by Artificial Fever Therapy."

### MICHIGAN

**New Unit at State Hospital.**—Construction has started on the second unit of the \$1,039,196 state hospital building program in Pontiac to provide accommodations for 700 additional patients. The new building will be located between the present administration building and the neuropsychiatric hospital, now under construction, and will house a general hospital unit. The neuropsychiatric unit will cost \$698,547. Financed partially by PWA funds, the building program at Pontiac is part of the \$11,000,000 state hospital building project.

**Guest Speakers in Wayne County.**—Dr. Daniel C. Darrow, associate professor of pediatrics, Yale University School of Medicine, New Haven, Conn., addressed a joint meeting of the Wayne County Medical Society and the Detroit Physiological Society in Detroit November 7 on "Salt Deficit—The Essential Feature of Clinical Dehydration." Dr. Martin E. Rehfuess, Philadelphia, addressed the medical section of the county medical society November 14 on "Gallbladder Infections" and Dr. Olga S. Hansen, Minneapolis, will speak before the surgical section November 28 on "Cardiac Problems in Pregnancy."—Dr. Eric M. Matsner, New York, gave an illustrated lecture November 1 before the Detroit Obstetrical and Gynecological Society; his subject was "Trends in Contraceptive Practice."

### MINNESOTA

**Protest Appointment of Physicians for City Employees.**—Over the protest of the Ramsey County Medical Society and the union of city and county employees, the city council of St. Paul appointed five physicians and surgeons to care for all city employees injured in line of duty. The medical society and the union contended that the plan infringed the right of

employees to choose their own physicians. Following the appointments the Ramsey County society adopted a resolution urging members to decline such appointments. In addition, the St. Paul Trades and Labor Assembly disapproved the plan and demanded that the Labor members of the council ask for a reconsideration. The medical society in its resolution pointed out that the state supreme court has held that an employee should have the unquestioned right to choose his medical attendant. In the same opinion it was held that the fact that the employer is a municipality and employs a physician cannot alter the construction of the statute. It was reported that three of the physicians appointed had refused to serve.

### MISSOURI

**District Meeting.**—The Eighth Councilor Medical Society was addressed in Joplin October 20 by Drs. James G. Carr, Chicago, on the syphilitic heart and Francis T. H'Doubler, Springfield, report of the International Goiter Conference in 1938. A symposium on treatment of accidental injuries was presented by Drs. Charles T. Reid, Joplin, on "The Eye and Highway Accidents"; Frank D. Dickson, Kansas City, "Roadside Emergency Care and Highlights on the First Dressing," and Donald F. Coburn, Kansas City, head injuries.

### MONTANA

**Personal.**—Dr. Leo F. Hall, formerly of Berea, Ohio, has been appointed health officer for Helena, and Lewis and Clark counties.

**Society News.**—Dr. Enoch M. Porter, Great Falls, has been elected president of the Montana Public Health Association and Dr. William F. Cogswell, Helena, reelected secretary for the twenty-fifth successive year, according to the *Journal-Lancet*.

### NEW YORK

**Society News.**—Dr. David M. Davis, Philadelphia, addressed the Rochester Academy of Medicine November 3 on "Prevention and Treatment of Serious Infections of the Kidney."—Drs. Rufus B. Crain and Morris E. Missal addressed the Rochester Pathological Society November 17 on "The Employee with Heart Disease—His Management in Industry."

**Farmer Convicted for Storing Marihuana.**—A farmer in Columbia County was fined \$400 and received a sentence to six months' imprisonment or, in lieu of the fine, another six months' imprisonment, for harvesting and storing marihuana. Bundles of the weed valued at \$1,500 were found in an attic. The case was settled by county and local police authorities under a special provision of the criminal code providing jurisdiction over misdemeanors applying to narcotic drugs.

**Graduate Courses in Syracuse.**—The medical education committee of the Onondaga County Medical Society is sponsoring the following graduate courses of several sessions each:

Diagnosis of Common Eye Diseases, Dr. Searle B. Marlow.  
Diagnosis and Treatment of the Commoner Types of Skin Diseases, Dr. Leon H. Griggs.  
Signs and Symptoms of Gastro-Intestinal Disorders, Dr. I. Harris Levy.  
Psychiatry in General Practice and the Specialties, Dr. Noble R. Chambers.  
Minor Surgery in General Practice, Dr. Edgar M. Neptune.  
Examination of the Central Nervous System, Dr. Wardner D. Ayer.  
Gynecologic Examinations in General Practice, Dr. Nathan P. Sears.

### New York City

**Typhoid Mary Is Dead.**—Mary Mallon, for many years known as "Typhoid Mary" because she was the first typhoid carrier identified in the United States and blamed for many cases before she was forced to live in isolation, died November 11 at Riverside Hospital. "Typhoid Mary" came to the attention of health authorities in 1904, when an epidemic of typhoid spread through Oyster Bay and adjacent towns. The disease was traced to a household where Mary had been a cook. She disappeared and was not discovered until 1907, when she was again found to be cooking in a Park Avenue home. After being proven to be a carrier she was committed to the hospital on North Brother Island to live. After three years the health department released her on her promise not to accept work in which food handling was involved. Four years later an epidemic occurred in a New Jersey sanatorium; Mary had been a cook there. Shortly afterward there was an outbreak at the Sloane Maternity Hospital with two deaths. She was sent then to the island permanently. She was about 70 years of age at her death.

**Science Writers Receive Award.**—The Clement Cleveland Medal of the New York City Cancer Committee was awarded at the annual dinner November 1 to the National Association of Science Writers "for outstanding work in the campaign to control cancer." Mr. William L. Laurence, science writer for the New York *Times*, received the medal for the association. The presentation was made by Mrs. Robert G. Mead, daughter of Dr. Cleveland, for whom the medal is named. Mrs. Mead is chairman of the cancer committee's finance committee. This was the second award of the medal, the first having gone to Henry R. Luce, publisher of *Time*, Inc., for the March of Time film on cancer. Dr. John C. A. Gerster, chairman of the cancer committee, presided at the dinner and presented to Mrs. Mead a book containing personal greetings from 225 friends and associates in recognition of her twenty-five years in cancer work. Dr. Francis Carter Wood presented a preview of the cancer exhibit which is to be shown at the New York world's fair in 1939. The exhibit will be on view at the Museum of Science and Industry until January.

**Society News.**—At a meeting of the New York Roentgen Society October 17 the speakers were Drs. Maurice N. Richter on "Experimental and Pathologic Aspects of Leukemia, Lymphosarcoma and Hodgkin's Disease"; Arthur P. Stout, "Indication for Surgery"; Albert Kean and Nathan Rosenthal, "Roentgenotherapy in Leukemia," and Maurice Lenz, "Roentgenotherapy of Lymphosarcoma and Hodgkin's Disease."

—At a meeting of the Medical Society of the County of Kings October 18 the speakers were Drs. Nathan B. Van Etten on "The Doctor Sits at the Crossroads"; Robert B. Osgood, Boston, "An Interpretation of the Principles and Proposals of the Informal Committee of Physicians (The Committee of 430)," and Irvin Abell, Louisville, Ky., President of the American Medical Association, "The Attitude of the American Medical Association Toward the Proposals of the National Health Conference."—Drs. James Alexander Miller and Adrian V. S. Lambert addressed the Brooklyn Thoracic Society October 21 on "Pathogenesis and Management of Pulmonary Tuberculosis" and "Surgical Treatment of Pulmonary Tuberculosis" respectively.—Dr. Harold E. B. Pardee addressed the Medical Society of the County of Queens October 21 on "Heart Disease and Pregnancy."

### OHIO

**New Health Commissioner in Cincinnati.**—Dr. Carl A. Wilzbach, executive secretary of the Cincinnati Social Hygiene Society, was appointed health commissioner of Cincinnati November 4 to take office not later than December 1. The city has not had an official commissioner since the death of Dr. William H. Peters in 1936, according to newspaper accounts. Dr. Owen C. Fisk was made acting commissioner after the death of Dr. Peters and later resigned because of ill health. Dr. Frank K. Harder succeeded Dr. Fisk as acting commissioner and will now become assistant commissioner. Dr. Wilzbach graduated from the University of Cincinnati College of Medicine in 1922.

**Advisory Council for Research Foundation.**—Announcement is made of the appointment of a scientific advisory council for the Children's Hospital Research Foundation, Cincinnati. The council consists of Drs. Oswald T. Avery of the Rockefeller Institute for Medical Research, New York; Ernest W. Goodpasture, professor of pathology, Vanderbilt University School of Medicine, Nashville, Tenn.; Albert Baird Hastings, Ph.D., professor of biological chemistry, Harvard University Medical School, Boston, and Alfred N. Richards, Ph.D., professor of pharmacology, University of Pennsylvania School of Medicine, Philadelphia. The Children's Hospital Research Foundation was established in 1929 with funds given by Mr. William Cooper Procter. The hospital and the foundation are affiliated with the University of Cincinnati College of Medicine, Dr. Albert Graeme Mitchell, professor of pediatrics, being director of the medical service at the hospital and of the foundation. Glenn E. Cullen, Ph.D., is director of laboratories. About 150 publications have appeared from the foundation staff.

**Society News.**—The industrial and orthopedic section of the Cleveland Academy of Medicine, the Bunts Institute and the Cleveland fracture committee of the American College of Surgeons sponsored a special meeting on fractures November 16. A clinic was held in the afternoon at St. Luke's Hospital, and Dr. John Albert Key, St. Louis, delivered the Bunts Lecture at the Cleveland Clinic in the evening on "Cervical and Trochanteric Fractures of the Femur."—Dr. Clyde E. Shinkle, Cincinnati, among others, addressed the Adams County Medical Society, Winchester, October 19 on infantile paralysis.—Dr. Parke G. Smith, Cincinnati, addressed the Clinton

County Medical Society, Wilmington, October 4 on "The Importance of Abnormal Renal Mobility."—Drs. Robert F. Thaw, Akron, and William M. Skipp, Youngstown, addressed the Portage County Medical Society, Atwater, October 6 on "Treatment of Diseases of the Ear, Nose and Throat" and "Problems Confronting the Medical Profession" respectively. —Bradley M. Patten, Ph.D., Ann Arbor, Mich., addressed the Mahoning County Medical Society, Youngstown, October 18 on "The First Heart Beats and the Beginning of the Circulation Studied Microcinematographically in Living Embryos." —Dr. Wiley D. Hickey, Leipsic, was elected president of the Northwestern Ohio Medical Association at its annual meeting in Defiance in October. Dr. Daniel B. Spittler, Hoytville, was made vice president and Dr. Frederic G. Maurer, Lima, secretary.

### PENNSYLVANIA

**Society News.**—Drs. William D. Stroud and Hugh Montgomery, Philadelphia, addressed the Northampton County Medical Society at the Country Club of Northampton County October 20 on "A Seven Years Study of the Clinical Efficacy of Various Digitalis Preparations" and "Treatment of Peripheral Vascular Disease" respectively. —Drs. John P. Griffith, Pittsburgh, and Walter M. Bortz, Greensburg, addressed the Westmoreland County Medical Society, Greensburg, October 18 on "Intestinal Obstruction" and "Hypertension" respectively. —Dr. William W. Bolton, Upper Darby, addressed the Medical Society of Lycoming County October 14 on "Syphilis Program of the Pennsylvania Department of Health." —Dr. Charles F. Geschickter, Baltimore, addressed the Cambria County Medical Society, Johnstown, October 7, on "Mammary Tumors."

### Philadelphia

**Personal.**—Florence B. Seibert, Ph.D., of the Henry Phipps Institute, University of Pennsylvania, received the honorary degree of doctor of laws from Goucher College, Baltimore, October 14, when the college celebrated its fiftieth anniversary.

**Ex-Residents' Annual Dinner.**—The fifty-second annual dinner of the Association of Ex-Resident Physicians of the Philadelphia General Hospital will be held December 6 at the Bellevue-Stratford. Dr. Randle C. Rosenberger, professor of preventive medicine and bacteriology, Jefferson Medical College, will be the guest of honor. Dr. Rosenberger was assistant pathologist at the Philadelphia General Hospital in 1898, when it was known as Blockley Hospital, and was director of the laboratory from 1903 to 1919. Dr. John J. Dailey, McAdoo, Pa., president of the association, will preside at the dinner. Ex-residents who do not receive notices of the dinner are requested to send their correct addresses to the secretary, Dr. George Wilson, 133 South Thirty-Sixth Street, Philadelphia.

**Society News.**—Drs. Norman R. Ingraham and John A. Kolmer addressed the Obstetrical Society of Philadelphia November 3 on "Treatment Reactions Among Syphilitic Pregnant Women with a Report of Seven Maternal Deaths from Syphilis Therapy" and "Syphilis in Relation to Gynecology and Obstetrics with Special Reference to Diagnosis and Treatment" respectively. —Dr. George P. Robb, New York, addressed the Philadelphia Roentgen Ray Society November 3 on "Visualization of the Cardiac Chambers, the Pulmonary Circulation and the Great Blood Vessels in Man." —Drs. Albert E. Bothe and Jonathan E. Rhoads addressed the Philadelphia Academy of Surgery November 7 on "Treatment of Kidney Tumors" and "Control of Hemorrhage in the Jaundiced Patient" respectively.

### TEXAS

**District Meeting.**—The Thirteenth (Northwest Texas) District Medical Society held a meeting September 13 at Breckenridge. The speakers included Drs. John Edward Johnson, Mineral Wells, "Gastric Failure in Middle Life"; William L. Marr, Galveston, "Treatment of the Anemias"; Truman G. Blocker Jr., Galveston, "Management of the Acute Traumatized Abdomen," and Herman P. Radtke, Fort Worth, "Fracture of the Neck of the Femur Treated by Internal Fixation."

### VIRGINIA

**Society News.**—Dr. Thomas S. Cullen, Baltimore, addressed the Norfolk County Medical Society, Norfolk, October 17 on sewage disposal and stream pollution. —Dr. Robert Finley Gayle Jr., Richmond, was the guest speaker at a recent meeting of the Medical Association of the Valley of Virginia in Staunton on "Treatment of the Psychoneurotic Individual."

**Lectures at the Richmond Academy.**—A series of lectures on the blood has been arranged by the committee on medical education of the Richmond Academy of Medicine. The series is as follows:

Harvey E. Jordan, Ph.D., Charlottesville, Embryology of the Blood, October 18.  
 Rolland J. Main, Ph.D., Richmond, Physiology of the Blood, November 1 and 15.  
 Dr. David T. Smith, Durham, N. C., Immunological Reactions of the Blood.  
 Dr. John H. Scherer, Richmond, Cellular Reactions Occurring in the Blood During Infections.  
 Dr. Frank L. Apperly, Richmond, The Pathologic Physiology of Anemia.  
 Dr. Maxwell M. Wintrobe, Baltimore, The Choice of Methods for the Correction of the Anemias and Why.

### WASHINGTON

**Society News.**—Dr. Herbert F. Traut, New York, addressed the Walla Walla Valley Medical Society, Walla Walla, November 14, on "The Present Status of Endocrinology Related to Gynecological Problems." Dr. Ralph H. Highmiller of the state department of labor and industry presented new changes in the accident fee schedule recently developed with the cooperation of the Washington State Medical Association. —Dr. Arthur M. Shipley, Baltimore, addressed the Spokane County Medical Society, Spokane, November 17 on "Surgical Conditions Involving the Diaphragm." Dr. Herbert F. Traut, New York, addressed a special meeting November 11 on "The Upper Urinary Tract in Pregnancy."

### WEST VIRGINIA

**Committee on Low Cost Medical Care.**—At a special meeting of the council of the West Virginia State Medical Association in Charleston October 2 a committee was appointed to formulate policies concerning prepayment or postpayment medical service plans or bureaus. Drs. Charles W. Waddell, Fairmont, president, and Ray M. Bobbitt, Huntington, president-elect of the state association, appointed the following committee: Drs. Robert J. Wilkinson, Huntington, chairman; John W. Moore, Charleston; Robert J. Reed Jr., Wheeling; Richard O. Rogers, Bluefield; Richard V. Shanklin, Gary, and Philip Johnson, Fairmont.

### GENERAL

**Urological Meeting.**—The Southeastern Branch of the American Urological Association will meet in Louisville, Ky., December 2-3. Among the speakers will be Drs. Herman L. Kretschmer, Chicago, on "Elusive Ulcer of the Bladder: A Critical Review of 110 Cases"; Joseph F. McCarthy, New York, "Prostatic Resection"; Charles C. Higgins, Cleveland, "Stone in the Urinary Tract," and Roger C. Graves, Boston, "Respiration Pyelography."

**Annual Meeting on Prevention of Blindness.**—The annual meeting of the National Society for the Prevention of Blindness will be held in New York December 1. Mr. Lewis H. Carris, managing director of the society, will give an address entitled "Thirty Years in Saving Sight" and the Leslie Dana Gold Medal will be presented to Dr. Ellice M. Alger, New York, who will speak on "Prevention of Blindness from the Ophthalmologist's Point of View."

**Propose Reunion of Workers on Brazilian Railroad.**—The Madeira-Mamore Association, composed of persons who worked on the construction of the Madeira-Mamore Railroad in central and western Brazil from 1907 to 1913, has proposed a reunion of all these workers during the world's fairs in 1939 in San Francisco and New York. Physicians and nurses who are not now members and who care to make themselves known can obtain information from John Y. Bayliss, Richmond, Va., president of the association; Edgar A. Smith, Newportville, Pa., secretary; John H. Armitage, 1205 Russell Road, Alexandria, Va.; Frank S. Jonas, 277 Broadway, New York, chairman of the New York committee, or Charles L. Dimmitt, Redwood City, Calif., chairman of the San Francisco committee.

**Society News.**—The first annual session of the American Medico-Legal Association will be held at the Drake Hotel, Chicago, May 12-13, 1939. Dr. Michel Pijoan, 137 Newbury Street, Boston, is the secretary of the association. —The Pan-Pacific Surgical Association will hold its third congress since its establishment in 1929 in Honolulu Sept. 15-28, 1939. Dr. Forrest J. Pinkerton, Young Building, Honolulu, Hawaii, is the secretary. —The Annual Midwinter Conference of Eastern Radiologists will be held February 10-11, 1939, in Washington, D. C., with headquarters at the Hotel Mayflower. For information, write the secretary of the local committee. Dr. Joseph F. Elward, 1726 Eye Street N.W., Washington.

**Fellowships Available for Research in Chemistry.**—Grants to the total amount of \$25,000 are available through the Lalor Foundation for research in any field of chemistry, according to an announcement. For a reasonable proportion of the awards, preference will be given to candidates "shaping their careers or carrying on research to accomplish a more effective application of the principles and discoveries of physical and organic chemistry upon problems of biochemistry, chemotherapy and pharmacology." The amount of each award will be determined on the basis of previous training, ranging usually between \$1,800 and \$2,500. Attainment of the Ph.D. degree or its equivalent in training is a requirement, but there are no other limitations as to age or residence. Inquiries and requests for application forms should be addressed to C. Lalor Burdick, secretary, Lalor Foundation, Wilmington, Del. The Lalor Foundation was established in 1935 for support of scientific research and has administered twelve fellowships. Applications must be filed by December 31.

**Tri-State Meeting.**—At the thirty-third annual meeting of the Tri-State Medical Society at the Grim Hotel, Texarkana, October 26-27 Dr. Joseph D. Roberts Jr., Longview, Texas, was elected president. The following were made vice presidents: Drs. Stanley George Wolfe, Shreveport, La.; Arley D. Cathey, El Dorado, Ark., and Richard G. Granbery, Marshall, Texas. Dr. Robert K. Womack, Longview, was elected secretary. The scientific program included:

- Dr. Walter G. Reddick, Dallas, Sulfanilamide in General Medicine.
- Dr. Stanley George Wolfe, Shreveport, La., Undulant Fever.
- Dr. Robert Lee Sanders, Memphis, Tenn., Surgical Treatment of Gallbladder Disease.
- Dr. Henry Gordon Rudner, Memphis, Synopsis of Medical Treatment of Gallbladder Disease.
- Dr. J. L. McGehee, Memphis, Preoperative and Postoperative Care of Abdominal Surgical Conditions.
- Dr. Oscar W. Bethea, New Orleans, A Study of the Status of New Drugs.
- Dr. Edward L. King, New Orleans, Diagnosis and Treatment of Cervical Dystocia.
- Dr. Lewis J. Moorman, Oklahoma City, Difficult Problems in Diagnosing Chest Conditions.
- Dr. Lee B. Harrison, St. Louis, Cardiovascular Syphilis.

**Western Surgical Association.**—The forty-eighth annual meeting of the Western Surgical Association will be held in Omaha December 2-3 with headquarters at the Hotel Fontenelle. The guest speaker will be Dr. William Boyd, Toronto, Canada, on "Tumors of the Neck." Among other speakers will be:

- Drs. Waltman Walters and Albert M. Snell, Rochester, Minn., Hemorrhagic Tendency in Jaundice, with Special Reference to Its Treatment with Vitamin K.
- Dr. Neil J. MacLean, Winnipeg, Man., An Improved Incision for the Radical Operation for Carcinoma of the Breast.
- Dr. George B. Packard, Denver, Indications for Splenectomy in Children.
- Dr. Henry W. Meyerding, Rochester, Minn., Diagnosis and Treatment of Ewing's Tumor.
- Dr. Stanley J. Seeger, Milwaukee, Technical Notes on Pediatric Surgery—(1) Hypertrophic Pyloric Stenosis and (2) Congenital Indirect Inguinal Hernia.
- Drs. George M. Curtis and Frank E. Hamilton, Columbus, Ohio, The Surgical Significance of the Motor Activity of the Human Stomach.
- Dr. Owen H. Wangenstein, Minneapolis, Experiences with Employment of Suction in the Treatment of Acute Intestinal Obstruction.
- Dr. William T. Coughlin, St. Louis, The Repair of Pharyngeal and Laryngotracheal Fistulae.

Dr. Casper F. Hegner, Denver, is president of the association.

**Special Society Elections.**—Dr. R. Wallace Billington, Nashville, Tenn., was elected president of the Clinical Orthopedic Society at its annual meeting in Nashville and Birmingham, Ala., October 7-8. Dr. Dale Wilson, Toledo, Ohio, was made vice president and Dr. H. Earle Conwell, Birmingham, secretary. Next year's meeting will be held in Little Rock, Ark., and Oklahoma City in October.—Dr. John C. McKinley, Minneapolis, was elected president of the Central Neuro-psychiatric Association at its annual meeting in Minneapolis October 7-8; Dr. Groves B. Smith, Godfrey, Ill., was made vice president and Dr. William C. Menninger, Topeka, Kan., secretary.—Dr. Herbert B. Wright, Cleveland, was made president-elect of the Aéro Medical Association at the recent annual meeting in Dayton, Ohio, and Dr. James C. Cole, New Orleans, was installed as president. Vice presidents at large elected were Capt. Harry G. Armstrong, Wright Field, Dayton; Drs. Richard H. Hoffman, Bellefonte, Pa.; Eldridge S. Adams, Washington, D. C., and Giles A. Coors, Memphis. Dr. Herbert F. Fenwick, Chicago, was elected first vice president and Dr. David S. Brachman, Detroit, reelected secretary.—At the thirty-ninth annual session of the Seaboard Airline Railway Surgeons Association in Richmond October 13-15 the following officers were elected: Drs. Arthur R. Beyer, Tampa, Fla., president; Joseph O. McClelland, Maxton, N. C., Robert O. Lyell, Miami, Fla., and Wilbur R. Bracey, Richmond, vice presidents, and Jarrett W. Palmer, Ailey, Ga., secretary.

## CANADA

**Professor Marrian Goes to Edinburgh.**—Guy F. Marrian, D.Sc., professor of biochemistry, University of Toronto Faculty of Medicine, Toronto, has been appointed to the chair of chemistry in relation to medicine at the University of Edinburgh. Professor Marrian was born in London in 1904 and educated at University College, London. After obtaining his doctor's degree in 1930 he was lecturer in the department of physiology and biochemistry at University College until 1933, when he received a William Julius Mickle fellowship from the University of London and went to Toronto as assistant professor of biochemistry. He was made a full professor in 1936.

**Society News.**—Dr. Frank A. Turnbull addressed the Vancouver Medical Association, Vancouver, October 4 on "Pituitary and Parapituitary Tumors."—Sir Edward Mellanby, secretary general of the Medical Research Council of Great Britain, gave an address at the University of Toronto October 5 under the auspices of the Canadian Medical Association. His subject was "Nutrition—Its Importance to the Individual and the Nation."—Dr. John Alexander, Ann Arbor, Mich., addressed the Academy of Medicine of Toronto November 1 in a joint meeting with district 11 of the Ontario Medical Association on "Management of Abscess of the Lung."

## Deaths in Other Countries

Sir Robert J. Johnstone, Newcastle, president of the British Medical Association in 1937, died October 26.—Dr. David Bruce Stewart Bruce-Jones, senior medical officer of the Canadian Pacific Steamship Line, died in London November 1.

## Government Services

### Training in Pathology and Diagnosis of Tumors

The surgeon general of the U. S. Public Health Service announces that, in order to meet the need for pathologists skilled in the diagnosis of tumors, special consideration will be given in making appointments for training under the provisions of the National Cancer Institute Act to qualified pathologists who wish to obtain additional training in diagnosis and pathology of tumors.

### Monthly Meeting of Navy Officers

Dr. Esmond R. Long, director of the Henry Phipps Institute of the University of Pennsylvania, Philadelphia, addressed the first monthly meeting of this season of the medical and dental officers of the navy at the Naval Medical School, Washington, D. C., October 10, on "The Use of Tuberculin in the Diagnosis of Tuberculosis."

### Residencies Open at St. Elizabeths Hospital

The U. S. Civil Service Commission announces open competitive examinations for internships and residencies at St. Elizabeths Hospital, Washington, D. C. It is expected that there will be two vacancies July 1, 1939, and two Oct. 1, 1939, for junior medical officers in rotating internships of two years; during the fiscal year beginning July 1, 1939, there will be five vacancies for psychiatric residents, graduate internships offered to graduates in medicine who have served an accredited internship. Applicants should state definitely whether they are applying for the rotating internship or the psychiatric residency. Entrance salaries are \$2,000 a year; if permissive legislation already proposed is passed by Congress, however, the salary of interns may be \$600 a year. All interns are required to live in the hospital and there are no quarters for the families of married interns. Applicants for the internships must be fourth year students in a grade A medical school and those for the residencies must have graduated from a grade A school and must have completed an internship of at least one year. Candidates must not have passed their fortieth birthday on the date of the close of receipt of applications. They will not be required to report at any place for examination but will be rated on the extent of their education and on the extent and quality of their experience. The closing date is December 13 for all except eleven states in the Far West, from which applications will be received until December 16. Forms may be secured from the Secretary, Board of Civil Service Examiners, at any first class post office, from the commission at Washington, D. C., or from any district office of the commission.

## Foreign Letters

### LONDON

(From Our Regular Correspondent)

Oct. 29, 1938.

#### Gas Masks for Babies and Young Children

Nearly two million gas masks for babies and young children are in course of construction. The problem of providing protection for them from gas attacks has proved difficult. They are being made in two sizes, one for children under the age of 2 years, the other for those between the ages of 2 and 4 years. Those for the older children are similar to adult civilian masks, but the uncomfortable straps are replaced by a neat rubber headpiece. Delay has been caused by the many experiments necessary before a suitable filter could be found through which children could breathe with ease. The masks for babies of 2 and under are an entirely British invention and have been designed differently from the ordinary mask. They fit over the baby's body and are secured between the legs.

#### The Danger of Naval Hospitals at Naval Centers

A correspondent of the *Times* points out that the chief naval hospitals are situated in important naval centers and that they might be seriously damaged in the event of bombardment or air attack. He therefore suggests that, in view of the difficulties of evacuating casualties by road or rail, hospitals should be placed in positions on the coast distant from any naval or military objectives, so that the transport of casualties might easily be effected by means of the small pleasure steamers at present to be found in holiday resorts. Such hospitals could be used as youth hostels in time of peace and readily converted to their purpose should hostilities begin.

#### Evacuation of Populous Areas in War

It is unfortunately true that war now means attacks on the civilian population of towns and cities. The government appointed a committee to consider the question of evacuation of populous areas in war and has accepted its report. The committee says that the whole issue in any future war may well turn on the manner in which evacuation from densely populated industrial areas is handled. People will be much safer in rural districts or in small country towns than in the heart of London. A thinning of the population of urban areas will relieve the pressure on essential services which might prove insufficient. In the event of an exodus, whether planned or forced by repeated air attacks, men and women engaged on essential work would in the great majority of cases be moved by a sense of duty to continue their tasks. The tendency to migrate would be especially among those who can be spared. The country will not be fully prepared until schemes of evacuation have been worked out for the main industrial centers and the necessary organization has been set up. The schemes must be on a basis of voluntary evacuation. Compulsory evacuation would arise only in limited areas subject to intensive bombardment or because of flooding or other reason they had become uninhabitable.

In the London area there appear to be adequate transport facilities for evacuation on any practicable scale. The main line railways would be fed by underground railways and busses. It is calculated that persons could be removed from London at a rate of 100,000 an hour. The refugees would have to be housed in private dwellings under a scheme of compulsory billeting. The Ministry of Health has assumed, as a rough basis for calculation, that five persons could be accommodated in every four rooms. A scheme of voluntary billeting is considered impracticable, but in the case of school children it would be an advantage if they were received as far as possible in houses that had expressed willingness to receive them. No serious difficulty is anticipated in feeding refugees provided arrangements are made in advance. Welfare services will be required and will offer a great scope for voluntary work. Chil-

dren should be transferred school by school and have the first claim on transport. The public should be educated in any scheme decided on.

#### The Destruction of Mosquitoes Carried by Airplanes

The possibility of airplanes introducing diseases into a country by carrying insect vectors from a place where it is rife must be provided against. Indeed, it has been stated that a new type of malaria was brought from Africa to Brazil in this way. There is now anxiety whether yellow fever, which has heretofore been confined to tropical America and Africa, will be transplanted to Asia. Imperial Airways maintains a research station in London, and experiments have been made there with a practically odorless and colorless vapor which is distilled from an English wild flower, pyrethrum, specially cultivated for the purpose. About 200 mosquitoes, all potential vectors of disease, were supplied by the London School of Tropical Medicine. The liquid distillate from the pyrethrum was poured into an atomizer constructed for use in aircraft, which was used in a room of about twice the capacity of the imperial flying boats. In seven minutes, about half the time during which the atomizer would be used on aircraft, all the insects were dead. The vapor is harmless to man but it will also kill the tsetse fly, the vector of trypanosomiasis. All countries through which Imperial Airways operates have regulations for preventing the carriage of disease by insects, but their regulations differ. It is hoped that international recognition of the method will be obtained.

#### The Need for a New Unity in Medicine

Opening the new medical school of the University of Aberdeen, Lord Dawson said that curative and preventive medicine were separated too much. At present preventive medicine was inadequately taught and was nothing but a postscript to the student's career. In recent years there had been a gradual growth of medical services and hospitals which, however individually excellent, were a medley of separate efforts. They fell under three headings: (1) communal services and clinics, (2) voluntary hospitals and (3) municipal hospitals. The communal services represented a fine achievement but had the serious defect of isolation and divorce from the general body of physicians in their district. The voluntary hospitals were centuries old and had grown up with the British people. To allow them to become absorbed by the local authorities into their municipal hospitals would be alien to our social evolution and a damage to our well being. But they could not stand as disconnected institutions and must play their part in a comprehensive scheme of medical services. They could not claim that the possession of teaching schools conferred the right to exclusiveness, for teaching had been extended to the communal clinics and municipal hospitals. The latter had come into existence during the last eight years and had steadily grown in numbers and importance. They were serving the community well but they should cooperate with the voluntary hospitals. Two sets of hospitals and two sets of doctors working independently would produce only confusion and conflict.

#### A "Trial Year" for Student Nurses

As stated in previous letters, the hospitals have difficulty in obtaining a sufficient number of nurses. The arduousness and restrictions of the profession deter girls from entering it. In some hospitals, hours of work have been reduced in order to increase the attraction. The West London Hospital has brought forward an entirely new scheme. Heretofore hospitals have not, as a rule, received girls for training under the age of 18, and a large number who leave school at 17 have to fill in a year before entering a nursing career. The West London Hospital proposes to fill this gap by providing training for girls as non-resident students who can get the hospital atmosphere and learn much of the work of the nurse. They will live at home and will wear overalls, not the nurse's uniform, at the hospital. There will be no restriction as to the use of cosmetics other than

good taste. At the end of the period the student will be free to decide whether she wishes to adopt the nursing career. Even if she does not she will not have wasted her time, for she will have learned much that is of practical use. The maximum hours of attendance will not exceed thirty in a five day week. Dinner and tea will be provided. Lectures will be given in the morning on hygiene, anatomy and physiology, invalid cooking, chemistry of foodstuffs, first aid and nursing. At the end of the course the students will sit for an examination and, if successful, will be accepted as probationers. At times some of the students will be admitted to the wards under the supervision of the sisters, but they will not be brought in contact with cases unsuitable for girls of their age.

## PARIS

(From Our Regular Correspondent)

Oct. 29, 1938.

### Annual Meeting of French Surgical Association

This year's congress of the French Surgical Association was held in Paris October 17-22, the date having been changed from October 6 on account of the recent international complications. The president of the present congress was Prof. Leon Imbert of Marseilles and the secretary was Professor Brocq of Paris.

#### TREATMENT OF RECENT CLOSED FRACTURES OF THE SPINE

The first subject chosen for reports and general discussion concerned the treatment of recent closed fractures of the spine. Drs. Charbonnel of Bordeaux and Sicard submitted the chief report on this question. Dr. Charbonnel's paper aimed to include only fractures of the bodies of the vertebrae without nerve complications. One's first duty is to attempt to educate the public how to transport a person whose spine is fractured. A great deal of harm may follow lifting the injured person by the shoulders or lower extremities. The best method is to place the patient face downward on a plank, a stretcher or a blanket supported at its four corners. If the injured person is found lying on the side or back, the utmost care should be taken in rolling him so as to place him face downward. Spontaneous reduction may take place if first aid is correctly applied. With the aid of a portable x-ray apparatus, films should be exposed without the patient being moved from his bed, as soon as possible after admission to a hospital. Both anteroposterior and lateral exposures must be made in order to give the surgeon essential information regarding the fracture. Both of the exposures can be made without the injured person being moved. Most frequently the dorsolumbar region, from the eleventh dorsal to the second lumbar vertebra, is involved. Even though the fracture be at a lower level, from the third to the fifth lumbar vertebra, the treatment is the same.

Based on a study of 217 cases without nerve complications, the results of the application of various nonoperative and operative methods show that the following conclusions can be drawn: The method of reduction termed hyperlordosis as advocated by Böhler should be employed as soon after the accident as possible. It aims only to place the upper and lower surfaces of the vertebrae parallel rather than to attempt to secure complete anatomic reduction. Many prefer placing the patient on the back rather than in the ventral position while reducing the fracture. No case has so far been reported of any serious nerve complication following the use of this method of reduction. The duration of the immobilization after reduction depends on the gravity of the fracture and the age of the patient. The Magnus method of permitting the patient to sit up in bed after four weeks and then encouraging him to walk unaided after six weeks of confinement to bed is applicable only to fractures with slight displacement and then only if the patient is under constant surveillance. The complete immobilization methods formerly employed are indicated at the present time only when the spinal injury is complicated

by fractures of the extremities. Even when the nonreduction method is used, a plaster cast in a position of lordosis followed by early physical therapy is indicated. Operative methods such as the use of bone grafts are seldom used for fractures of the spine without nerve involvement because the results are not as satisfactory as with the Böhler method of early reduction for fractures in the dorsolumbar region. The use of bone grafts at an early period is to be recommended only in comminuted fractures of several adjacent vertebrae, oblique fractures which show rapid displacement following early reduction and plaster cast, and so-called fracture-dislocations without nerve complications, if orthopedic methods are unsuccessful.

#### TREATMENT OF FRACTURES OF THE SPINE WITH NERVE COMPLICATIONS

The second half of the report was presented by Dr. Sicard of Paris. As to the relative frequency of spinal fractures with nerve complications, he had been able to find 195 cases, or 42 per cent, of fractures with nerve complications as compared to 467 without such a complication. Nerve lesions are most common in fractures involving the last cervical and first few dorsal vertebrae. At present, no clinical sign is pathognomonic of a complete involvement of the spinal cord. A complete, flaccid paralysis, the Babinski sign in extension, the defensive reflexes and the law of Bastian all lack absolute value. Histologic study of traumatic cord lesions teaches that the spinal cord does not possess the property of regeneration. Only three clinical signs can give an approximate evaluation of the severity of the lesions. These are (a) early and persistent priapism, (b) early edema of the lower extremities and (c) the rapid appearance of trophic changes such as decubitus over the sacrum or heels. When these are observed within a few days after the injury, they indicate complete destruction of the cord.

Some surgeons believe that, if the cord is destroyed, operative intervention is of no avail. If there is some lessening of the paralysis, efforts to maintain the integrity of the muscular and joint systems are all that are indicated. Others advocate immediate reduction, hoping that the decompression will lessen the damage to the cord, or they recommend laminectomy as a routine procedure. A third group has no fixed plan but tries to combine different methods of treatment. The conclusions of the author were that no treatment is of any avail if the cord is completely divided. The only hope of any improvement is that the symptoms may be only the result of an edema. Between these two extremes of opinion as to treatment one should not remain inactive in a case of fracture of the spine, complicated by paralysis, contrary to former teaching. The lesion should be regarded as curable and treatment begun as early as possible, either by reduction of the fracture or by laminectomy, the only contraindications being the existence of severe shock or the necessity of caring for a more urgent injury. In partial paralyses, reduction is always to be recommended, controlled at intervals by radiography and supplemented by early physical therapy. In complete paralyses, especially of the spasmodic type, reduction is followed by rapid recession of symptoms. If the paralysis is of the flaccid type, it is more difficult to decide on the indications. The most reliable diagnostic method is radiography. The presence of a bone fragment in the spinal canal, persisting after reduction, calls for laminectomy. Operation is indicated also if the articular processes are impacted. In general, if no amelioration of symptoms has taken place in from eight to fifteen days an exploratory laminectomy is justifiable. The higher the level of the fracture with nerve complications, the less favorable the prognosis. A flaccid paralysis is always to be regarded as a grave sign, indicating irreparable lesions.

The discussion was opened by Dr. Schotte of Ghent, Belgium, who advocated early reduction in the dorsal position.



In the treatment of cases with nerve root symptoms the first step should be epidural or paravertebral anesthesia in order to exclude cases of a purely functional character, so frequently encountered in malingerers in industrial surgery. Dr. Charles Mayer of Brussels, on the basis of a follow-up study of eighty-six personally observed cases, seventy without and sixteen with nerve complications, believed that orthopedic reduction can be regarded as a decided step in advance especially in cases with nerve complications. In the absence of such symptoms, reduction is indicated if the film indicates a crushing injury involving more than a fourth of the height of the vertebral body, especially in younger persons. If orthopedic reduction is correctly employed, indications for the use of bone grafts will rarely be encountered. Laminectomy should be done if the signs of cord injury appear late or recur after temporary recession. Dr. Lambret of Lille also endorsed the efficacy of early reduction as advocated by Böhler. Professor Leriche of Strasbourg said that there is no disagreement as to the value of immediate reduction in cases of moderate severity but that there is a divergence of opinion as to its application in the severe type. In the latter, if the nerve complications do not improve after reduction, immediate laminectomy is indicated, preceded by cystostomy to prevent kidney infection following catheterization.

#### STAPHYLOCOCCIC SEPTICEMIA

The second question for reports and general discussion was the clinical forms and treatment of staphylococcic septicemia. Dr. Jean Patel of Paris placed the staphylococcic septicemias as observed clinically in three groups, the acute, subacute and chronic forms. The first of these includes two subgroups. In the first the clinical picture is that of an acute infection in which it is impossible to find an atrium, a diagnosis becoming possible only after positive blood and urine cultures. In the second subgroup the general symptoms are as marked as in the first subgroup but a local lesion such as a furuncle, especially one on the lip or in the nose, precedes the onset of the symptoms of septicemia. In some cases in this second subgroup, after two or three days of severe general symptoms an acute osteomyelitis or multiple skin localizations attract attention to the existence of a general staphylococcic infection. In the second main group, the subacute, the clinical picture of a generalized sepsis shows signs of recession at a time when evidences of metastatic infection, in the form of osseous, articular, muscular, cutaneous and even pulmonary or renal foci, appear. In the third principal group, the chronic form of staphylococcic septicemia, the patient gives a history of recurrent staphylococcic localization in the form of furuncles, pulmonary or perinephric abscess or suppurative prostatitis.

As to the laboratory side of the question, animal experiments fail to reproduce the clinical pictures. The staphylococcus is carried by way of the veins, and inoculation of animals is followed by rapid metastatic foci. The staphylococcus secretes a toxin which possesses lethal properties toward all the cells of the body, although giving rise to the rapid formation of an antitoxin. The staphylococcus, far from being destroyed by the leukocytes, retains its virulence and is transported by the white blood cells through the venous circulation to the right ventricle, then to the lungs and left ventricle, and finally to the systemic circulation. The defensive agents are the opsinins and lysins, less often the leukocytes. The clinical picture is due to the direct action of the bacteria rather than to their toxin, except in the case of necrotic lesions which are the result of the action of the toxin.

The treatment of staphylococcic septicemia was the subject of a report by Dr. Moiroud of Marseilles, who reviewed the nonoperative measures, placing them in three principal groups. The first includes transfusions, which can stimulate blood formation and phagocytosis. As to immunotransfusions, their value is not settled. Although some favorable results have

been obtained in some cases, in many others immunotransfusion has failed. The danger of shock and of dissemination of the infection as the result of transfusions of any form, must not be overlooked. The shock (foreign protein) treatment appears to be rational but is not to be recommended because of the danger of starting up a true septicemia. The same criticism can be made of the use of vaccines and of toxoids, the latter recommended by Ramon. If staphylococcus toxoid is employed, a preliminary test should always be made of the sensitivity of the patient. The bacteriophage treatment should be used only locally because the intravenous injection may be followed by serious symptoms. Chemotherapy, the use of acriflavine hydrochloride or mercurochrome, has given some good results if these products are employed in very minute doses. The operative treatment aims to clear up the atrium of infection but often it is impossible to find one.

The discussion was opened by Prof. Robert Debré, who stated that a true staphylococcic septicemia is rare as compared with transitory bacteremias, which are common. Recent studies show that the staphylococcus acts as the result of formation of a toxin rather than because of its virulence per se, and hence more is to be expected by giving specific antitoxins and toxoids than from any other treatment.

#### BERLIN

(From Our Regular Correspondent)

Oct. 17, 1938.

#### The Development of Neuroses

The last few decades of medical research have taught us to revise our concepts of the neuroses. The diagnosis of "psychopathies" of various types is purely descriptive. On the other hand the concept of neuroses, which has grown up around psychotherapeutic experience, takes into account the many predisposing factors which underlie a manifestation of abnormal psychic development and reactivity, and hypothesizes that, granted correspondingly favorable circumstances, many neurotic persons would have remained healthy. Accordingly, it is considered that through psychotherapy one afflicted with a neurosis may be restored to mental health. The entire problem was recently summarized by Prof. J. H. Schultz, Berlin neurologist, who is thoroughly conversant with the field and who is the author of several books on neurosis. The hypothesis of heritability and improvement remains uncorroborated by genetic research; severe congenitally characterologic deficiencies are not classified as neuroses. A special difficulty in the field of neuroses lies in the fact that identical clinical syndromes may be based on wholly disparate anamneses. It is therefore impossible to establish a distinctive pathology of the nervous disturbances of heart action, speech, sleep, volition and so on. Rather an attempt must be made to identify the neuroses according to their development and to determine the "principal psychologic field of its source."

A classification of the neuroses, suggested by the author, is here of further assistance.

Since a neurosis or psychopathy is to be considered a developmental disturbance, a defective and morbid adaptation to life, all possible fundamental causes of such a maladjustment should be passed in review. Schultz places in his first category mental disturbances in which the patient has been completely dependent on another sick or otherwise afflicted person. For example, if the infant of an abnormal or inferior mother reacts to the situation by neurotic manifestations it is plainly not the child but the mother who requires treatment. The child should be transferred to a wholesome milieu, where in a brief time it will become normal. The neuroses (of the children) in such cases are termed by Schultz fremdneurosen (exogenic neuroses); they are produced exogenically and based on allopsychic conflicts. In such cases it is not at all a question of special individual psychotherapy but of active supervision and above all change of environment.

Then there are the neuroses of bad habit, for example, nictitation based on childhood conjunctivitis with photophobia. Schultz says that these neuroses are physiogenic and as they are situated to a certain extent on the borders of personality he terms them *randneurosen* (marginal neuroses). For this group a complicated treatment based on a profound study of the personality is superfluous and useless; a simple active therapy will suffice.

It is otherwise with those neuroses which, psychogenic in the usual clinical sense, are based on normally experienced emotions such as grief, distress, anxiety or jealousy. As the "middle strata" of the psyche are disturbed in the neuroses Schultz terms them *schichtneurosen* (stratum neuroses). These originate (preponderately) in endopsychic conflicts. Various methods of therapeutics, none of which may be called genuine psychotherapy, are here applicable.

On the other hand, major psychotherapy is indicated only in the really severe neuroses. Since in the latter the "nucleus" of personality is altered, Schultz terms them the nuclear neuroses. It is possible to be affected with an exogenic, a marginal or a stratum neurosis and still retain a fairly sound general personality. But in a characterogenic nuclear neurosis the entire personality "has been" neurotically deformed from earliest childhood and a state of autopsychic conflict has been constantly present. In such cases the personality of the patient must be gradually reeducated, consciously and subconsciously, through a painstaking course of profound psychotherapy, which will need to continue for months or years. Schultz warns against a summary exclusion of the possibility of a nuclear neurosis in cases which present bronchial asthma, insomnia, anxiety states and so on; this is often done because the manifestations appear "too mild." Such symptoms may mask a deep-seated nuclear neurosis of wide ramifications. If a neurosis remains refractive to minor psychotherapeutic measures, it must never be concluded that psychic factors are not present; rather, says Schultz, an approach by major psychotherapy should be essayed whenever feasible.

### ITALY

(From Our Regular Correspondent)

Oct. 30, 1938.

#### Insurance of Health of Workers

The Italian journal *Difesa Sociale* recently published statistics on the clinical and social work which has been carried on by the Istituto della Previdenza Sociale during the last year on laborers. The department of insurance against tuberculosis began functioning in 1929. During the year 9,345 persons were given medical care in hospitals of the department. Every year the number of those who are cared for by the department increases. The insurance against tuberculosis protects peasants as well as laborers. New hospitals and sanatoriums have been made available and the laboratories for diagnosis have been properly equipped. The department cared for 37,099 insured persons or members of their families in 1936 and 44,420 in 1937, with a total number of 8,565,023 days of hospitalization for the whole group.

The department of insurance against invalidism sent 15,796 insured persons or members of their families in 1936 and 20,720 in 1937 to have treatments at balnearies of mineral waters. The department manages fourteen balnearies, four of which are the property of the department. In the course of 1937, 4,997 convalescents of diseases which may cause invalidism were sent to sanatoriums for convalescents which are run by the department, with a number of days of sojourn of 141,746 for the whole group. The Institution for Social Providence has fifty-three trachoma dispensaries for both insured and noninsured persons. There were 24,500 trachomatous patients who were observed and treated in 1937. Consultations and treatments numbered about 1,265,445. The insurance to protect motherhood covers peasant women as well as laboring women. The department has seventeen offices for consultation, in which about 27,614

consultations from about 10,429 were given in the course of 1937. The mothers are cared for in the course of pregnancy, labor and the puerperium and are given guidance with regard to nursing their babies.

#### Temperature and Pulse of White People in the Tropics

Dr. Semmola, lieutenant of medical officers in Somaliland, took the temperature and determined the pulse rate in 600 normal healthy Italian soldiers in Somaliland. They have lived for some time in tropical zones under good hygienic conditions and they are well protected against the severity of the climate. The determinations were made early in the morning and at noon. The atmospheric temperature varied between 86 and 95 F. The humidity was between 60 and 70 per cent. The axillary temperature was above 98.6 F. in 28 per cent of the cases, but the subjects were in normal health. The author believes that the temperature of the body of normal white persons is physiologically increased in tropical lands and that the increase has no pathologic significance. The pulse rate in tropical lands is normal in the morning (from 70 to 74 beats a minute) and increased at noon (from 80 to 84 beats a minute).

### POLAND

(From Our Regular Correspondent)

Oct. 22, 1938.

#### Arterial Blood Pressure in Diseases of the Eye

In the Ophthalmologic Clinic of Warsaw University Professor Lauber and Dr. Sobański have found that serious disorders of the eye can be due to a disproportion between blood pressure and intra-ocular pressure. The disproportion can result from an increase of intra-ocular pressure or from a decrease of blood pressure. The imbalance of both these pressures may cause an insufficient supply of blood to the retina and to the optic nerve. This phenomenon is exemplified in the development of optic nerve atrophy in *tabes dorsalis*. In this disease, optic nerve atrophy progresses gradually as the blood pressure sinks and stops or progresses more slowly when the blood pressure increases. Constitutional arterial hypotension or hypotension caused by antisyphilitic therapy provokes a greater involvement of the eye in tabetic patients. Hypotension in the retinal arteries was found not only in *tabes dorsalis*, but also in many "idiopathic" cases of atrophy of the optic nerve and in pigmentary degeneration of the retina. These facts are important in the therapy of *tabes dorsalis* for controlling atrophy of the optic nerve. In every case of *tabes dorsalis* the proportion of the arterial to the intra-ocular pressure has to be controlled either by increasing the former or by decreasing the latter. The decrease of intra-ocular pressure is more safely and easily obtained than is an increase of blood pressure. In every case the authors instilled pilocarpine or physostigmine and, if its effect on the intra-ocular pressure was not sufficient, cyclodialysis was performed. After the prevention of eye involvement, antisyphilitic treatment was begun. The effect of antisyphilitic therapy on blood pressure has to be constantly watched and in case of a great decrease of blood pressure it has to be stopped. The authors suggest that in most cases of *tabes dorsalis* serious eye complications can be prevented if adequate prophylactic measures are taken.

#### The Number of Physicians in Poland

According to the official report of the Polish Medical Chamber, the total number of physicians practicing in Poland was 12,215, or one physician for 2,833 inhabitants. The percentage of Jews among the physicians is about 33.4, while Jews are only 9.6 per cent of the whole population in Poland. Among the chief causes of deaths of physicians in the last year were cardiovascular diseases 40.5 per cent, tuberculosis 17 per cent, malignant tumors 13 per cent, epidemic diseases 8 per cent and suicide 4 per cent.

### Tuberculosis in Children

Dr. T. Mogilnicki read a paper before the Warsaw Pediatric Society on the incidence of tuberculosis in children in Poland. His data are based on researches on tuberculosis in various districts in children in the elementary and high schools, in nurseries and in children from 1 to 6 years of age. In the schools attended by poor children the Pirquet test was positive in 38 per cent in children of 6 and in 44 per cent in children of 7 years, while in schools attended by rich children the Pirquet test was positive in 18 per cent in children of 6 and in 19 per cent in children of 7. In the Jewish children the percentage of positive Pirquet tests was higher by more than 10 than in Christian children. This test is more frequently positive in children in large cities than in rural children in the West of Poland. In the East of Poland, where the financial conditions of the rural population are worse, the Pirquet test is more frequently positive in the country than in cities. The author determined the total number of tuberculous children in Poland to be about 370,000. The tuberculosis mortality of children at the age of 1-5 years is high in Poland, being 38 per cent as against 5.7 in Germany, 5.0 in Denmark, 15.0 in Estonia, 12.0 in France, 8.2 in Norway and 7.3 in Sweden per 10,000 of the population of this age. These researches on tuberculosis in children have shown that the most frequent source of infection is tuberculous persons in the environment of the children. The author believes that the poor state of health of the young generation in Poland is mainly due to an inadequate campaign against tuberculosis by the government, resulting from inadequate funds. He urges the x-ray examination of school children and teachers in order to isolate the tuberculous subjects as sources of infection and to be able to start treatment in early stages of the disease.

### CAPE TOWN

(From Our Regular Correspondent)

Oct. 12, 1938.

### The Medical Congress

Last month the Medical Association of South Africa (British Medical Association) held its thirty-second medical congress at Lourenço Marques, Portuguese East Africa, for the first time in its history beyond the borders of the Union of South Africa. The meeting was held at the invitation of the health services of Mozambique and under the patronage of the Portuguese minister for colonies, Dr. Francisco Viera Machado. It was an unqualified success and was attended by doctors from the Union of South Africa, Rhodesia, Angola and the Portuguese colonies. Thus there was an opportunity to discuss matters of common interest. An attractive program of entertainment, including native dances, open air fetes and excursions to the game reserves, somewhat interfered with the excellent professional program, but the sectional and plenary meetings were well attended and the discussions, in Portuguese and English, were animated and instructive. From the old Portuguese universities of Coimbra and Lisbon, delegates attended, among them being the deans of faculties of medicine, who contributed interesting papers. The president of the congress was Dr. Vasco Palmeirim, chief of the local department of health, and the organizing secretary was Dr. Abel de Carvalho, a local radiologist. Among the most interesting papers were those on malaria by Professor Froilano de Melo of Nova Goa, on heliotherapy by Professor Grober of Jena, on bronchopulmonary suppuration by Dr. Nunes de Almeida of the Instituto Portugues de Oncologia of Lisbon, and on the extracardiac arteries in the circulation of the myocardium by Prof. Maximino Correia of Coimbra. The discussions on the nutritional problems of the natives were interesting, while one plenary session was devoted to discussion of the treatment of peptic ulcer, the consensus favoring conservative treatment as against gastrectomy and emphasizing that gastric and duodenal ulcers are not merely local lesions. Another instructive session was devoted to com-

parative medicine. Since 1928 the medical association has invited the veterinary surgeons to participate in the congress, and the combination has been mutually advantageous. At this congress Dr. Gilles de Kock of the research institute at Onderstepoort, which is associated with the memory of Sir Arnold Theiler, contributed a paper on the role assumed by game and wild animals in the spread of human disease. Both the Union of South Africa and Mozambique are keenly interested in their game reserves. The present outbreak of foot and mouth disease and the possibility that the larger antelopes and wild bovines might be carriers of disease enhanced the interest in the discussion. A second paper, on the risks of introducing yellow fever by airplanes, was read by Dr. Park Ross, who demonstrated his method of disinfection by means of a special spray. The next congress will be held at Port Elizabeth next year but will be overshadowed in importance by the congress of 1941, when the British Medical Association will hold its annual meeting, jointly with the South African Association, at Johannesburg. An organizing committee has already been appointed to make preliminary arrangements for that meeting.

### Rickettsiosis

Pijper and Crocker, from the former's private laboratory at Pretoria, have made an intensive study of rickettsiosis in South Africa, the results of which they have published. The three types—tick bite fever, murine or rat flea or sporadic typhus, and louse typhus—prevalent in the country are considered to be a group by themselves. They have come to the conclusion that South African typhus is not identical with classic typhus from their extended study of the serologic differences in the agglutinin titers of a large number of rabbits infected with the Basutoland strain of epidemic typhus. They found a sporadic typhus virus immunologically identical with a virus in rats that protected against tick bite fever but not against epidemic typhus. This sporadic form of typhus dies out in guinea pigs when brain injections are used, while the epidemic form can be kept indefinitely by this method.

### Smallpox and Amaas

The relationship between smallpox and the type of it locally known as amaas, which appears to have affinities to the type known in Europe as alastrim, has long been a matter of controversy. A posthumous paper by Dr. George Hay is devoted to the clinical and epidemiologic features of amaas. The author concludes that the natives penetrated into the northern Transvaal in two separate streams, which have not intermingled until recent times. The southern group shows evidence of infection by genuine classic smallpox; the northern group shows signs of infection by a smallpox-like disease that leaves little scarring and disfigurement. Both types are readily controlled by vaccination, but the author suggests that the vaccine used should contain strains of both types, particularly that of the light or amaas type. Vaccination, although compulsory by law, has been much neglected, with the result that the non-immune population is rapidly increasing.

## Marriages

- PAUL LE ROY MARTIN, Skykomish, Wash., to Miss Evelyn Rosetta Goodenough, July 24.  
ROBERT E. NELSON to Miss Margaret Hoffman, both of Harrington, Wash., August 26.  
EDWIN G. LEE, Colfax, Wash., to Miss Elrina Ellerbrock of Los Angeles, July 12.  
VERNE W. RITTER to Mrs. Blanche Bullock Burns, both of Seattle, August 6.  
EDWIN S. WEISFIELD to Miss Mildred Schonfeld, both of Seattle, August 4.  
TAMARA J. KABALKIN, Seattle, to Mr. Arthur Sternoff, July 15.

## Deaths

**Patrick Eugene McSweeney** ☉ Burlington, Vt.; University of Vermont College of Medicine, Burlington, 1886; past president of the Chittenden County Medical Society and the Vermont State Medical Society; adjunct professor of obstetrics at his alma mater, 1895-1914, instructor of gynecology, 1900-1903, professor of gynecology, 1911-1925, professor of obstetrics, 1914-1925, and since 1925 emeritus professor of obstetrics and gynecology; member of the New England Obstetrical and Gynecological Society and the New England Surgical Society; fellow of the American College of Surgeons; attending surgeon to the Bishop de Goesbriand Hospital, Burlington, Fanny Allen Hospital, Winooski, and the Porter Hospital, Middlebury; consulting gynecologist to the Mary Fletcher Hospital; aged 76; died, September 2, of diabetes mellitus, chronic myocarditis and hypertension.

**Ernest Coleman Levy**, Richmond, Va.; Medical College of Virginia, Richmond, 1890; professor of histology, pathology and bacteriology at his alma mater, 1897-1900, and in 1925 was professor of preventive medicine; health officer of Richmond, 1906-1917, and director of public welfare, 1919-1924; health officer of Tampa, Fla., 1925-1928; served during the World War; charter fellow and past president of the American Public Health Association; past president of the Richmond Academy of Medicine and Surgery; author of numerous papers on public health topics; aged 70; died, September 29.

**Julius C. Le Hardy** ☉ Major, U. S. Army, retired, Port St. Joe, Fla.; University of Georgia Medical Department, Augusta, 1893; veteran of the Spanish American and World wars; served as a reserve officer on active duty for many years; entered the medical corps of the regular army as a first lieutenant in 1927 and retired in the same year under a special act of Congress approved March 3, 1927, for disability in line of duty; in 1930 was retired as a major under act of June 21, 1930; aged 67; died, September 3, of a self-inflicted bullet wound.

**George Newton Bell**, West Hartford, Conn.; Yale University School of Medicine, New Haven, 1892; member of the Connecticut State Medical Society and the New England Surgical Society; fellow of the American College of Surgeons; consulting surgeon to the Hartford, Hartford Isolation and Mount Sinai hospitals, Hartford; Litchfield County Hospital, Winsted, Home for Crippled Children, Newington, Memorial Hospital, Manchester, Rockville City Hospital, Rockville, Bristol (Conn.) Hospital; aged 68; died, September 10, of cerebral hemorrhage.

**Russell Sturgis Rowland**, Detroit; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1901; member of the American Pediatric Society and the American Academy of Pediatrics; was awarded a silver medal for his excellent presentation of studies on lipid metabolism at the annual meeting of the American Medical Association in Detroit in 1930; on the staffs of the Children's, Harper and Woman's hospitals; aged 64; died, September 29, of cerebral thrombosis.

**Wesley Harold McKnight**, Bedford, Ind.; Indiana University School of Medicine, Indianapolis, 1922; member of the Indiana State Medical Association; past president and secretary of the Lawrence County Medical Society; served during the World War; on the staff of the Dunn Hospital; aged 42; died, September 9, in the Passavant Memorial Hospital, Chicago, of acute bacterial endocarditis.

**James Edward Neighbors** ☉ Poughkeepsie, N. Y.; Vanderbilt University School of Medicine, Nashville, Tenn., 1920; on the staffs of the Vassar Hospital and St. Francis Hospital, Poughkeepsie, Sharon (Conn.) Hospital, Butterfield Memorial Hospital, Cold Spring and St. Benedictine Hospital, Kingston; aged 40; died, September 13, in St. Luke's Hospital, New York.

**Edward Schnaper** ☉ New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1895; fellow of the American College of Surgeons; gynecologist to the Lebanon Hospital and consulting obstetrician to the New York Nursery and Child's Hospital; aged 63; died, September 3.

**Daniel Stevens Latham** ☉ Cranston, R. I.; Medical School of Maine, Portland, 1893; for many years health officer; at one time served in the house of representatives and later in the state senate; formerly a member of the school committee; aged 71; died, September 21, of coronary thrombosis.

**Robert Edwin Holmes**, Harrisburg, Pa.; Eclectic Medical Institute, Cincinnati, 1894; member of the Medical Society of the State of Pennsylvania; at one time member of the state

board of medical education and licensure; for many years on the staff of the Harrisburg Polyclinic; aged 78; died, September 6.

**Archie J. McDowell**, Soldiers Grove, Wis.; Milwaukee Medical College, 1898; member and past president of the State Medical Society of Wisconsin; formerly member of the state legislature; for many years president of the board of education; aged 74; died, August 28, of peritonitis and strangulated hernia.

**William Alexander Hackett**, Detroit; University of Toronto Faculty of Medicine, 1894; member of the Michigan State Medical Society; fellow of the American College of Surgeons; on the staff of St. Joseph's Mercy Hospital; aged 70; died, September 16, of carcinoma of the urinary bladder.

**Woodrow Charles Pickering**, Columbus, Ohio; Ohio Medical University, Columbus, 1901; member of the Ohio State Medical Association; for many years police and fire department physician; aged 64; died, September 22, in the Grant Hospital of acute monocytic leukemia.

**Guy Seward**, Fremont, Neb.; Barnes Medical College, St. Louis, 1902; member of the Nebraska State Medical Association; veteran of the Spanish-American and World wars; aged 64; died, September 6, in the Nicholas Senn Hospital, Omaha, of cerebral thrombosis.

**Worthington Seaton Russell** ☉ Woodbury Falls, N. Y.; University of the City of New York Medical Department, 1893; at one time an acting assistant surgeon with rank of lieutenant junior grade in the U. S. Navy; aged 68; died, August 16, of coronary occlusion.

**Louis Alden Pindler** ☉ Los Angeles; University and Bellevue Hospital Medical College, New York, 1920; on the staff of the White Memorial Hospital; aged 45; died, October 9, in the Lincoln Hospital of an infection resulting from a splinter in his hand.

**William Edward Gorman**, Springfield, Mass.; Atlantic Medical College, Baltimore, 1909; aged 69; on the staffs of the Mercy Hospital and the Wesson Hospital, where he died, September 9, of cerebral thrombosis, left hemiplegia and arteriosclerosis.

**Harold David Haney**, Western State Hospital, Tenn.; University of Tennessee College of Medicine, Memphis, 1934; member of the Tennessee State Medical Association; on the staff of the Western State Hospital; aged 29; died, September 13.

**Herman Walter MacDonald** ☉ Newcastle, Ind.; Indiana University School of Medicine, Indianapolis, 1909; on the staff of the Clinic Hospital; aged 55; died, September 21, in the Robert W. Long Hospital, Indianapolis, of peritonitis.

**Frank Willis Almond** ☉ Boise, Idaho; McGill University Faculty of Medicine, Montreal, Que., 1919; served with the Canadian Army during the World War; county health officer; aged 50; died, August 26, of coronary thrombosis.

**Edward Francis Brennan**, Norwood, Mass.; Tufts College Medical School, Boston, 1908; member of the Massachusetts Medical Society; formerly chairman of the school committee and board of health; aged 54; died, September 9.

**Butler Hall Sanchez**, Plant City, Fla.; Atlanta Medical College, 1914; member of the Florida Medical Association; served during the World War; aged 51; died, September 21 at St. Joseph's Hospital, Tampa, of pneumonia.

**Frank Alonzo Kirby** ☉ New Haven, Conn.; Columbian University Medical Department, Washington, D. C., 1895; aged 68; died, September 5, in Grace Hospital, of toxic purpura following transfusion and pernicious anemia.

**Walter C. Head**, Bessemer, Ala.; Birmingham Medical College, 1901; past president of the board of education; member of the Medical Association of the State of Alabama; aged 63; died, September 3, of carcinoma of the pancreas.

**David Wallace Mott**, Los Angeles; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1881; formerly member of the state senate; at one time mayor of Santa Paula, Calif.; aged 83; died, August 26.

**Albert Morton Shaw** ☉ Nauvoo, Ill.; Medical College of Ohio, Cincinnati, 1890; formerly secretary of the Hancock County Medical Society; aged 73; died, September 13, in Burlington, Iowa, of pyelonephritis.

**William D. Brydone-Jack**, Vancouver, B. C., Canada; L.R.C.P., L.R.C.S., Edinburgh, 1884; formerly coroner; for many years on the staff of the Vancouver General Hospital; aged 78; died, September 1.

**Rubert Stewart Royce**, Brooklyn; University of Vermont College of Medicine, Burlington, 1889; member of the Medical Society of the State of New York; aged 72; died, August 16, of angina pectoris.

**Francis W. McNamara**, Chicago; Chicago Medical College, 1889; for many years county jail physician; aged 71; died, September 16, in the Presbyterian Hospital of cerebral hemorrhage.

**Thomas Blanchard Herrick** Ⓢ Manson, Iowa; State University of Iowa College of Medicine, Iowa City, 1912; served during the World War; aged 52; died, September 2, of coronary thrombosis.

**Ernest Bonner**, Camden, Ala.; Bellevue Hospital Medical College, New York, 1898; member of the Medical Association of the State of Alabama; aged 63; died, September 19, of myocarditis.

**Leonard A. Muns**, Smithfield, N. C.; College of Physicians and Surgeons, Baltimore, 1885; aged 76; died, August 30, in the Johnston County Hospital of a fracture of the hip and pneumonia.

**Francis Paul Kean MacMurrough**, Jersey City, N. J.; St. Louis College of Physicians and Surgeons, 1886; served during the World War; aged 73; died, September 6, of heart disease.

**Edward Levis Prizer**, Southern Pines, N. C.; Harvard University Medical School, Boston, 1912; aged 53; died, September 7, of hypertrophic arthritis, chronic nephritis and uremia.

**Brown Lee Pursifull**, McKee, Ky.; St. Louis College of Physicians and Surgeons, 1920; aged 43; died, September 2, in the Veterans Administration Facility, Lexington, of pneumonia.

**Homer C. Behymer**, Amelia, Ohio; Eclectic Medical Institute, Cincinnati, 1895; aged 69; died, September 1, in St. Francis Hospital, Cincinnati, of arteriosclerosis and heart disease.

**Victor Josephson** Ⓢ Chicago; College of Physicians and Surgeons of Chicago, 1894; aged 70; died, September 11, of coronary thrombosis and arteriosclerotic heart disease.

**William Roy Johnston**, Natchez, Miss.; Howard University College of Medicine, Washington, D. C., 1902; aged 60; died September 6, of encephalitis lethargica and influenza.

**Perry Xavier Martin Jacobs**, Cincinnati; Cincinnati College of Medicine and Surgery, 1899; aged 66; died, September 12, of diabetes mellitus and cirrhosis of the liver.

**Robert H. Jacobs**, Joppa, Ill.; Kentucky School of Medicine, Louisville, 1894; served during the World War; aged 71; died, September 9, in Metropolis of paralysis agitans.

**Jane Orr**, Oakland, Calif.; Tufts College Medical School, Boston, 1901; member of the California Medical Association; aged 69; died, August 19, of coronary sclerosis.

**William Porter Moore**, College Grove, Tenn.; Vanderbilt University School of Medicine, Nashville, 1894; aged 65; died, September 1, of complications following typhoid.

**Harry Parke Beatty**, Chicago; University of Wisconsin Medical School, Madison, 1930; aged 33; died, September 4, of injuries received in an automobile accident.

**Albert Herman Lazere** Ⓢ Sioux City, Iowa; University of Illinois College of Medicine, Chicago, 1931; aged 35; died, September 8, of carcinoma of the stomach.

**Burton Willis Swayze**, Allentown, Pa.; Jefferson Medical College of Philadelphia, 1891; aged 70; died, August 1, in the Sacred Heart Hospital of carcinomatosis.

**Nathaniel Burwell**, Shepherdstown, W. Va.; University of Maryland School of Medicine, Baltimore, 1907; died, September 16, of pulmonary tuberculosis.

**Atchie M. Nicks**, St. Joe, Ark.; Memphis (Tenn.) Hospital Medical College, 1888; aged 75; died, August 28, of valvular heart disease and arthritis.

**Morris Leon Loevenson**, Chicago; College of Physicians and Surgeons, Baltimore, 1893; aged 76; died, September 27, of carcinoma of the stomach.

**Oliver Perry Erwin**, Medora, Ill.; Missouri Medical College, St. Louis, 1887; at one time mayor; aged 75; died, September 5, of cystitis.

**Augusta Nordell Carlson**, Boston; Boston University School of Medicine, 1914; aged 58; died, August 15, of diffuse cerebral sclerosis.

**Hugh Jenkins**, Tucson, Ariz.; Rush Medical College, Chicago, 1881; aged 81; died, September 19, of acute nephritis.

**Nelson Potter**, St. Louis; Barnes Medical College, St. Louis, 1905; aged 75; died, September 6, of uremia.

## Correspondence

### PRACTICAL MEDICAL ECONOMICS

*To the Editor:*—I have been able to make substantial financial progress in the past two years without increase in gross income and in spite of the business "recession" and even decrease in gross income during the past fourteen months, in a manner which could be used with profit and satisfaction by any harassed practitioner. There are few, if any, practitioners whose gross incomes would not allow them to live respectably and save money for old age if the practitioner did not make so many mistakes in management.

Record keeping is a great help. I got out the records of the people who had been guilty of gross nonpayment of obligations since 1925. The social and economic history of every one of these families and people was reviewed to see, principally, whether we had done a charitable act in serving them without being hard boiled about the pay. The result of the analysis was enlightening and profitable. Just about 5 per cent of these account losses were to people who could not pay at that time or any other and who deserved to be helped. The remaining 95 per cent were people whose protestation of poverty was a misrepresentation. They paid for their groceries, automobiles, gasoline, liquor, tobacco, vacations and everything else except their medical service. Location in a small community where one is able to know what the patients are doing when they are not ill, and how they live, has its analytic advantages. For the most part, the average individual's or family's claim that they cannot afford or pay for good medical service is not substantiated in fact. I have become so sensitized to the type and approach of the patient with the false claim of poverty that the first step of such an individual across the consultation room threshold and the first glance decide the credit problem, right there and then. Practitioners have for so many years been the dupes of every unscrupulous deadbeat, and still are, that a great many of the present (and threatening future) economic troubles of the profession arise from this. Having given so much so easily, the practitioner is now asked to give more.

Another fallacy is the inferiority complex-induced idea that it is necessary to "keep up with the Joneses." Most of the things that the Joneses do are an unmitigated bore and an offense to a moderately active intellect, besides, for the most part, being plain stupid. The entire family is much happier since we stopped purposely and energetically pursuing happiness at the bridge club, the golf course and over the social alcohol, and lived a more rational life. I have come to agree with a well known psychiatrist who expressed his conviction that the most of the wild pursuit of pleasure was but a fugue, an attempted flight from reality.

In another way I have saved money: I have gotten so that I can throw the average drug salesman, specialty salesman, instrument and gadget salesman out of the office without the least compunction whatever. Some of the salesmen were indignant, but I take notice that after these salesmen's day's work is done they go home or to their hotel and sit down and worry about their own troubles and not about mine, and why should I worry about theirs? This leads to the corollary that many practitioners have much too much of the wrong kind of equipment and many many too many pills, liquids, ointments and plasters, all of which cost them good money. Which also leads to the observation that it is not necessary to load the patient up with several kinds of medicine he does not need just to make him think you are doing something for him and to keep him satisfied. Many practitioners believe this semihumbog practice is necessary, but the conviction arises from the physi-

cian's lack of sufficient self respect and lack of confidence that his therapy is correct and the best available for the case at the time.

Another important way I have straightened out financial affairs comes under the head of "Trust no future, howe'er pleasant, let the dead past bury its dead, act, act in the living present, heart within and God o'erhead" (Longfellow), which, applied to medical practice, means Do not wait for future and perhaps never eventuating increased prosperity to plan your budget, savings and old age security. If increased income and prosperity come, fine, but in the meantime figure that life will be ever thus and plan accordingly. The average, well perhaps not the average but far too many, physicians are intending to plan their lives next week or next month or next year. Well, that time never comes, and they go on and on and on and on and know not where they are going. But I know where they are going. They are going where all unpractical fools deserve to go, physician or any one else. Do you remember Dickens's Micawber? When it was too late he philosophized: Income of five crown three shilling and expenditures of five crown five shilling, result misery; income of five crown three shilling and expenditures of five crown one shilling, result happiness.

GEORGE W. WILLIAMSON, M.D., Dundee, Mich.

## Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

### RESTORATION OF PATENCY OF OVIDUCTS

*To the Editor:*—A woman aged 30 is desirous of becoming pregnant. Pregnancy occurred at the age of 27 but was interrupted because of financial considerations she says, although I think there was some other reason. She has been advised as to the physiologic period and repeated efforts have been made. The tubes were recently tested for patency with air up to 200 mm. of mercury pressure and also with iodized oil and pictures were taken. The pictures reveal patency only to the fimbria with no leakage in the abdominal cavity. Is there a retrograde procedure whereby these tubes can be opened? Please give references to a description of this and your opinion on its results.

M.D., Florida.

**ANSWER.**—Transuterine inflation with air or gas, commonly known as the Rubin test, is the only nonoperative measure that might open the obstructed tubes. This procedure, primarily employed for diagnosis, results in reestablishing patency, followed by pregnancy in a modest percentage of cases.

Abdominal operative intervention has been looked on with greater favor during recent years, particularly in cases such as the one described.

### NO WAY TO INCREASE HEIGHT OF ADULT

*To the Editor:*—A man aged 29 is 5 feet 4 inches (163 cm.) tall and weighs 120 pounds (54 Kg.). He is in good health but comes every day to ask if it is possible for him to grow at least 5 inches more. I tell him it is impossible, but he insists, saying he read in an American paper about a pituitary gland extract and a certain class of exercises for increasing height. Is this possible?

A. JARAMILLO, M.D., Colombia, South America.

**ANSWER.**—In the present state of medical knowledge we know of nothing capable of adding 5 inches in stature to a patient 29 years of age. In all probability this patient's growth was completed from eight to ten years ago. Attempts at the present time at increasing height through the use of pituitary extract are more apt to lead to symptoms of acromegaly than to increased height. Perhaps the taking of a roentgenogram of the wrist and a demonstration that ossification has been completed, together with an explanation as to why no further growth is possible, would serve to satisfy the patient's mind. Once the epiphyses have joined the shaft of the long bone, growth is complete so far as height is concerned. Exercise likewise offers nothing; neither does a combination of exercise and endocrine products.

### EXTRACTS FROM FOODS FOR CUTANEOUS TESTS

*To the Editor:*—What is the best way to obtain dried protein extracts from foods for the cutaneous testing of allergic patients? Here in Mexico we have only those extracts prepared in the United States and since we have many foods unknown in that country, I am interested in obtaining the protein extracts from those foods.

LUIS PEREZ PARRA, M.D., Guadalajara, Mexico.

**ANSWER.**—The simplest method for obtaining atopens is that of extracting and drying the fresh food. Those foods which contain the juice require no solvent. The material is placed in a grinder or juicer. The juice obtained is filtered through filter paper and may then be dried either by passing a current of air over it or preferably under negative pressure in a vacuum desiccator containing sulfuric acid or some other dehydrating agent. In this group it is best to select ripe or nearly overripe fruits or vegetables, so that the pectin content may be at a minimum. Materials that contain little or no juice should be ground thoroughly and soaked in distilled water with frequent shakings for several days. During this period a small amount of toluene should be used as a preservative. The solution should then be dried as described.

Materials rich in fats require extraction with anhydrous ether after grinding and before aqueous extraction. This method, while simple, usually gives gummy material even after thorough drying. The nature of the substance, however, does not interfere with scratch tests.

Another method, which however requires considerable laboratory apparatus and training, consists of allowing the juice or extraction to fall, drop by drop, into acetone kept at minus 20 C. The final proportion of the material added to the acetone should not be more than one part of the material to nine parts of the acetone. The acetone is then filtered off and the precipitate is dried in a desiccator and then ground in a mortar. Solid carbon dioxide (dry ice) may be used in the acetone for keeping the temperature at minus 20 C. or below.

### DISCOVERY OF PHENOLPHTHALEIN AS LAXATIVE

*To the Editor:*—How and where was phenolphthalein discovered to have laxative properties? Is this dye ever used in the making of wine?

M.D., New Jersey.

**ANSWER.**—The laxative value of phenolphthalein was discovered by Zoltan von Vamossy, who published the paper announcing it in *Therapie der Gegenwart* 4:201 (May) 1902.

The story usually goes that the Hungarian government decided to use phenolphthalein for the denaturing of wine made from the husks of grapes. These artificial wines are made by adding sugar water to the pressed husks of grapes and allowing the mass to ferment. Soon after the law went into effect, it is said, a mysterious diarrheal disease overtook a large proportion of the poorer inhabitants of Hungary, which, it was discovered, was due to the denaturant, phenolphthalein. This story is disputed by Vamossy, who says that it is "unfair to the Hungarian government to think that it would have permitted anything to be added to any drink without previously investigating its effect on the health of the people."

Vamossy also says "That the laxative properties of this drug could not possibly have been discovered by the drinking of adulterated wines may be noted from the following: Phenolphthalein turns pink in an alkaline solution even in a dilution of one to ten millions, and as the amount of phenolphthalein that is needed to detect these wines is infinitesimal (0.1 Gm. to 100 liters), it would be necessary, even if 1 Gm. were used, to drink at least 10 liters of the wine before diarrhea would develop."

This, Vamossy says, is the true story of its discovery:

"When it was proposed to denature artificial wines with phenolphthalein, I was first entrusted with the task of investigating the harmlessness of this reagent. I carried on numerous experiments on animals with negative results. One small pet dog that received 6 Gm. of phenolphthalein became quite constipated and passed fecal masses as if it had been on a diet of bones, but these fecal masses became crimson on the addition of alkali. Following this the drug was tried on man. A colleague took 1 Gm. and I took 1.5 Gm. of phenolphthalein at 11 a. m. The effect appeared between 1 and 3 p. m. that afternoon, in the form of three to five watery evacuations accompanied by some borborygmi. A similar action occurred that evening and also the next morning but in no way disturbed us from our regular afternoon laboratory work or our night's rest. I became convinced that I had discovered a laxative of merit. It was easy to take owing to its tastelessness. It did not gripe and did not seem to have any drastic effect even in large doses (1.5 Gm.). It was later found that 0.1 Gm. taken in the evening emptied the contents of the colon the following morning, resulting in a copious but soft movement."



## VOMITING AND HIGH EXTERNAL TEMPERATURE

*To the Editor:*—A boy aged 10 years complains of itching, nausea and a sensation of heat during warm weather. These are followed in several days or weeks by vomiting. When he rides in a car to the hospital, 30 miles, the vomiting is stopped but he complains of being hot until he is given dextrose intravenously, which helps him. The attacks are not associated with fever, constipation or diarrhea. After the vomiting spells he has an enormous appetite for several weeks. As an infant he was given several formula diets and finally S M A and later Dryco. He could not take cow's milk until he was 2 years old and always had either constipation or diarrhea. When  $2\frac{1}{2}$  he had diphtheria and vomiting spells at intervals lasting between four and ten hours. At about 4 years of age he had vomiting and convulsions and intestinal infection during a spell of extremely hot weather ( $118^{\circ}$  F. for four days). During the subsequent two summers he was at the beach, where it was cool, and had several slight spells and continued to itch at intervals. When 6 years of age he had infantile paralysis and vomiting, from which he recovered without much paralysis but was left extremely nervous. In the summer of 1937, when 9 years old, he complained of a sensation of heat, itching and headache. He rode horseback in the mountains but had a vomiting spell, after which the appendix was removed. Five weeks later there was more vomiting and hemorrhage. He was given dextrose intravenously. In February 1938 he started vomiting blood, which was checked by dextrose intravenously. He had a similar attack May 21, 1938. The temperature where he lives is dry and hot, between 105 and 110. When taken out of this climate to the coast, where it is damp and cool, he has improved promptly. He gives a positive cutaneous test to casein, lactalbumin, orange, eggs, tomatoes, carrots, spinach, cabbage, corn, lima beans, bananas, beets, radishes, grapes, raisins, apricots, artichokes, chocolate, chicken and mustard. Any suggestions for diagnosis and treatment will be appreciated.

M.D., California.

**ANSWER.**—The heat-regulating mechanism of infants and children is more labile than that of adults. The symptoms enumerated in the history of this boy are rather vague but simulate the injurious effects of heat. The cutaneous eruption is probably also an effect of the high external temperature. As the patient was relieved by summering on the coast, it would seem that this is the most rational form of therapy for him.

## ETIOLOGY OF GLAUCOMA

*To the Editor:*—I have recently read an article entitled "The Symptomatology of Glaucoma and the Problem of Pathogenesis," by André Magitot, translated from the original articles in the *Annales d'oculistique* (166:356 [May], 439 [June], 565 [July], 609 [Aug.] 1929) by Hallard Beard. In some respects this article is so very different from sections on glaucoma in such books as Berens' and Gifford's recent textbooks for students that I am wondering whether the ideas presented in Magitot's article are commonly accepted by American ophthalmologists.

M.D., Nebraska.

**ANSWER.**—The series of articles by Magitot represents a somewhat individual point of view which is not shared in most of its essentials by the majority of ophthalmologists. His view represents a reaction from the older view that glaucoma is always due to an obstruction of the chamber angle. It is now admitted that a vascular factor plays a part in some cases, especially in acute glaucoma; but obstruction of the chamber angle is still considered an important factor. His view that chronic glaucoma should be treated by general measures is not accepted by most ophthalmologists, since the results of operations which secure more efficient filtration are known to be successful in the majority of cases. There is a great deal of other evidence that obstruction of the filtration angle cannot be neglected in glaucoma.

## CORNEAL ULCER FROM CATALIN?

*To the Editor:*—A patient has had a corneal ulcer. He was employed by a firm using catalin for plastic products and has been struck in the left eye on several occasions with catalin. Could this be a predisposing cause? What is the action of catalin on the cornea?

M.D., Massachusetts.

**ANSWER.**—Catalin is a synthetic resin, produced by the chemical combination of phenol and formaldehyde. It has the general appearance of honey and may be molded into suitable shapes to produce the desired manufactured objects. Solidification takes place as a result of curing, which is induced by heating. The completed objects are extremely hard and in some respects resemble bakelite, in others synthetic resin. Catalin products may be given a wide variety of colors as a result of the addition of aniline dyes. In some instances a rainbow or marbled effect may be desired, which may mean that several aniline dyes have to be utilized. Finished catalin products are apparently harmless, but in the manufacture of catalin numerous injuries have taken place, chiefly involving the eyes. In *Industrial Hygiene*, a publication of the Department of Labor of New York State (15, August 1936) there may be found an extensive discussion of the manufacture; use

and toxic properties of catalin. In the investigation there reported, it was noted that 55 per cent of the workers examined presented nondisabling conjunctivitis and 11 per cent an inflamed nasal mucosa and that more than 94 per cent presented some evidence of irritation of the upper respiratory tract. Industrial dermatitis was not detected. Workers examined complained that the entry of foreign bodies into their eyes was common and troublesome. Further, complaints were encountered as to eye discomfort, lacrimation and photophobia. However, these conditions were noted chiefly when workmen left the workpoint at the end of the day or at noontime, and particularly the eye complaints were more noticeable in colder weather.

In view of the fact that catalin is a known eye irritant, leading chiefly to low grade conjunctivitis, it is reasonable to believe that it might play some part in the occurrence of corneal ulcers. It may be believed that particles of larger sized dust entering the eye may have constituted a more direct factor in initiating the ulcer, which in turn may have been aggravated as a result of the irritant properties of the vapors of formaldehyde and phenol, if exposure to these was present.

## HAND INJURY

*To the Editor:*—Three months ago a woman aged 56 was struck on the dorsal surface of the right hand at the middle of the second metacarpal bone by a piece of glass falling from the seventh floor of a building. She received a small laceration and her hand was swollen for about three weeks. The wound healed by first intention and a small almost invisible scar remains. As a result of the injury the second and third fingers are much smaller than the corresponding fingers of the left hand; they are held slightly flexed and cannot be entirely straightened. Motion is decidedly limited, the patient being unable to close her hand completely. The skin over the fingers is tight and glistening. The fourth and fifth fingers also are involved but to a lesser extent. She complains of numbness over the dorsal surface of her second and third fingers. Her fingers are sensitive to cold. X-ray examination was negative at the time of the accident and a picture taken three weeks ago also was negative. What is the explanation of this change?

M.D., West Virginia.

**ANSWER.**—There was partial or complete division of the cutaneous branch of the radial nerve, of the common extensor tendons and possibly of the extensor indicis proprius. The scar tissue that formed helps to fix the injured tendons and to prevent complete extension and to restrict flexion. The same scar tissue interferes with the return flow of blood and return flow of lymph along the lymphatic channels and accounts for the poor circulation and sensitiveness to cold.

## EFFECT OF SKIN TUBERCULOSIS ON PULMONARY TUBERCULOSIS

*To the Editor:*—Does the presence of an associated cutaneous tuberculosis influence favorably the prognosis of pulmonary tuberculosis? Kindly list references on this subject.

M.D., New York.

**ANSWER.**—All observations and reports indicate that cutaneous tuberculosis rarely exists in fatal pulmonary tuberculosis but rather in conjunction with extrapulmonary disease. Wail (Inverse Relation Between Tuberculosis of the Skin and Tuberculosis of the Internal Organs, *Virchows Arch. f. path. Anat.* 277:115, 1930) and Memmesheimer (Influence of Cutaneous Tuberculosis on Pulmonary Tuberculosis, *Skin Clinic, Essen*, June 1936), among others, bear this out in their reports. It must not be assumed too hastily, however, that this is due to activity of the skin alone. While the skin seems to have a decided immunizing effect, the peculiarity of the bacilli that localize in the skin or other extrapulmonary organs must also be considered.

There are instances, however, in which bacilli of full virulence and typical behavior have appeared to yield to collateral skin infections. These effects cannot be explained satisfactorily on any other basis than as a result from stimulation of the skin.

Perhaps the most important report on this subject is that of Zinn and Katz (Biologische Einwirkung von der Haut auf den gesunden und tuberculösen Organismus, *Tuberculose-Bibliothek*, 1927, No. 27), who show that the skin is an organ subject to various stimuli and that definite immunizing properties originate in the skin as a result of chemical, bacterial or light stimuli. They cite the work of Petruschky, Moro, Ponnendorf and a host of others in which dead bacillary extracts were injected into the skin for immunization effects.

Kutschera (Therapy of Severe Pulmonary Tuberculosis by Artificial Production of Cutaneous Tuberculosis, *Wien. klin. Wchnschr.* 50:1547 [Nov. 12] 1937) has recently gone further and applied the principle in the use of living bacilli inoculated into the skin of tuberculous patients. Various protective anti-

bodies have been demonstrated after such inoculations. He recommends this procedure in various forms of slowly progressive secondary type of pulmonary tuberculosis, in which group he has made more than 1,000 inoculations without ill results. Primary tuberculosis inoculations, however, must scrupulously be avoided.

#### BLEPHAROCALASIS

*To the Editor:*—A white man aged 28 complains of a narrowing of his left palpebral fissure. He has been aware of this for at least three years. No pain and no disturbance of vision are associated and there are no headaches. In 1934 the left eye was edematous, mostly in the surrounding tissues. An eyeground examination then revealed a slight hyperemia, which appeared to follow the ingestion of strawberries. In forty-eight hours the edema subsided. In 1932 the patient suffered from a pansinusitis. Treatment consisted of irrigations of the left frontal sinus and both maxillary antrums. There was an uneventful recovery except for a postnasal discharge. At present examination reveals no inflammation of the lids or conjunctiva. The left upper eyelid is slightly edematous. Its edge covers the uppermost portion of the iris. There is a perceptible narrowing of the left palpebral fissure; there are no extra-ocular palsies and the eyegrounds are normal. Visual acuity of the left eye is 20/30 (Snellen), of the right eye 20/20. The serologic reaction is negative; neurologic examination and x-ray examination of all sinuses are negative. What are the possibilities? Will an angioneurotic edema last so long? In 1934 when the acute episode occurred, two ophthalmologists and two nose and throat men concurred in that diagnosis. I have noted several persons with a similar abnormality. The patient has shown me a photograph of himself at the age of 2. There is a suggestion of a slight narrowing of the left palpebral fissure. After loss of sleep the abnormality seems to be accentuated.

M.D., North Carolina.

*ANSWER:*—Apparently the case described is a condition known as blepharochalasis. This is usually the result of repeated attacks of acute edema of the lids resembling angioneurotic edema, but with a peculiarity of the connective tissue in the lid which leaves a thinned and pendulous upper lid. It is sometimes associated with vasomotor rhinitis during acute attacks. Efforts to trace it to some form of allergy have not been successful. It is necessary in many cases to resect a portion of skin in order to correct the overhanging portion of the lid. Shrinking of the nasal mucous membrane and the use of ice seem to help as much as anything.

#### PYELITIS AND FEVER

*To the Editor:*—Would diathermy be efficacious in the treatment of chronic pyelitis in a woman 30 years of age? The urine is usually negative for bacilli. I have been treating her with pyridium (0.2 Gm. daily taken before retiring). She has a fever every day of 99.6 F. between the hours of 11 a. m. and 4 p. m. only. Does the fever at these hours signify anything unusual?

M.D., New York.

*ANSWER:*—Diathermy is seldom of any value in the treatment of pyelitis. In the case mentioned it would seem important to submit this patient to a thorough urologic investigation in order to rule out the possibility of any obstruction in the urinary tract. If the examination is entirely negative, the use of mandelic acid or sulfanilamide should be highly efficacious in eradicating the existing infection. The occurrence of fever at the hours mentioned does not appear to have any significance.

#### FACIAL PALSY FROM TRAUMA

*To the Editor:*—A boy aged 8 fell from a tree 4 feet off the ground and hit his head; he did not lose consciousness and apparently was not hurt; from two to three days later he complained of soreness on the left side of his face and his mother noticed a paralysis on that side. I examined him one week after the fall; there were no symptoms of a fractured skull and x-ray examination shows none. A physical examination discloses a paralysis of the left side of the face; I did not test him with the faradic current. After four weeks there has been no change in his condition and I am interested in finding out whether anything can be done at present to restore function and when a plastic operation should be indicated if the condition fails to improve. I may add that the boy apparently was in perfect health before the accident and has been since it occurred.

M.D., Texas.

*ANSWER:*—The history suggests fracture of the skull which has injured the facial nerve or direct trauma to the nerve. The muscles of the face should be supported by an adhesive splint attached to the cheek and forehead. The boy should have massage and daily stimulation with the galvanic current as well as exercises in which he attempts to use that side of the face. If there is no return of function in the muscles of the face within three months, an anastomosis of the facial nerve and the hypoglossal and spinal accessory nerves should be considered. In the interim, the muscles of the face must be kept from relaxing and this is best accomplished by a splint.

#### DIVERTICULITIS OR CARCINOMA

*To the Editor:*—Can you outline for me or refer me to literature discussing the present status of diverticulitis and diverticulosis particularly with regard to its treatment? A white woman aged 61 came to me several months ago complaining of a loss of 40 pounds (18 Kg.) during the preceding eight months, accompanied by symptoms of weakness, anorexia, nausea and occasional vomiting. With the exception of a hemoglobin of 65 per cent, the blood and urine were normal. Physical examination was essentially negative. A gastrointestinal study disclosed an extensive diverticulitis. Treatment with a milk, cream and egg diet, barium sulfate powder orally and liquid petrolatum have been continued for about one month with little improvement in the anorexia and nausea, her most persistent and distressing symptoms. If she could achieve a normal food intake, her secondary symptoms would probably subside.

HOWARD G. BOSLAND, M.D., Verndale, Minn.

*ANSWER:*—The history as given suggests the probability of carcinoma. In about one third of the cases of diverticulosis complicated by sigmoiditis there is carcinoma, which is not revealed by an x-ray examination. Hence it may be wise to have surgical consultation. Diverticula of the colon are best handled with a low residue, high vitamin diet, and low olive oil retention enemas containing a small amount of aristol powder. Sufficient liquid petrolatum should be given by mouth to keep up the bowel movements.

#### References:

- Brown, P. W., and Marcley, D. M.: Prognosis of Diverticulosis and Diverticulitis of the Colon, *THE JOURNAL*, Oct. 23, 1937, p. 1328.  
Willard, J. H., and Bockus, H. L.: Clinical and Therapeutic Status of Cases of Colonic Diverticulosis Seen in Office Practice, *Ann. J. Digest. Dis. & Nutrition* 3: 580 (Oct.) 1936.  
Drueck, C. J.: Diverticula and Diverticulitis, *Rev. Gastro-Enterol.* 4: 134 (June) 1937.  
Dixon, C. F.; Deuterman, J. L., and Weber, H. M.: Diverticula of Intestine, *Surg., Gynec. & Obst.* 66: 314 (February, No. 2A) 1938.

#### GENTIAN VIOLET FOR ORAL LESIONS

*To the Editor:*—Of what value is gentian violet in lesions of the mouth, such as trench mouth? What is the best strength of solution to use for young children?

J. C. FRYE, M.D., Williamsburg, Pa.

*ANSWER:*—Gentian violet has been widely used in the treatment of various oral lesions but reports of its efficiency vary greatly. Aqueous solutions of gentian violet are nontoxic and nonirritating and yet can kill or inhibit the growth of many of the gram-positive bacteria of the mouth. Gentian violet is occasionally advocated for the treatment of Vincent's infection (trench mouth). Probably gentian violet would improve general oral hygiene as much as any other mild antiseptic and hence would have some beneficial effect on cases of Vincent's infection. However, oxidizing agents such as hydrogen peroxide and sodium perborate are usually more effective. Gentian violet is probably more valuable in the treatment of thrush and other fungous infections of the mouth. A 0.5 to 1 per cent aqueous solution of gentian violet may be used with safety on young children. A description of gentian violet and related rosaniline derivatives appears in New and Nonofficial Remedies, 1938, pages 218-221.

#### MACERATION OF FETUS

*To the Editor:*—What is the shortest time in which the skin of a dead fetus might become macerated? I delivered a stillborn infant at term with a tight knot in the cord. It was so macerated that the skin rubbed off on the slightest touch. Yet the mother thought she had felt life within twenty-four hours of the birth.

H. O. SKINNER, M.D., St. Paul.

*ANSWER:*—The skin of a dead fetus can macerate in a short time. It is entirely possible to have extensive maceration within a twenty-four hour period. Many factors influence the rate of maceration. Heat and infection are the most common of these factors. In the presence of one or both of these, marked maceration can occur within several hours.

#### LEGISLATION FOR DESTRUCTION OF RAGWEED

*To the Editor:*—In *Queries and Minor Notes* in *THE JOURNAL*, Oct. 8, 1938, page 1397, is a discussion of legislation concerning the destruction of ragweed. In this connection it is noteworthy that the sanitary code of the city of East Orange, N. J., received an additional amendment Oct. 5, 1933:

"That any thing, condition or act which is or may become a detriment or menace to human health and the following specific things, conditions and acts are, each and all of them, hereby declared to be and are defined as nuisances:

" . . . (g) Permitting ragweed in the flowering state to be or to grow upon any public or private property."

Health Officer.

F. J. OSBORNE, East Orange, N. J.

## Medical Examinations and Licensure

### COMING EXAMINATIONS

#### STATE AND TERRITORIAL BOARDS

**ALABAMA:** Montgomery, Jan. 3-5 and June 20-22. Sec., Dr. J. N. Baker, 517 Dexter Ave., Montgomery.

**ALASKA:** Juneau, March 2. Sec., Dr. W. W. Council, Box 561, Juneau.

**ARIZONA:** Basic Science. Tucson, Dec. 20. Sec., Dr. Robert L. Nugent, Science Hall, University of Arizona, Tucson.

**COLORADO:** Basic Science. Denver, Feb. 7-8. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver. Medical. Denver, Jan. 4-6. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

**CONNECTICUT:** Basic Science. New Haven, Feb. 11. Prerequisite to license examination. Address State Board of Healing Arts, 1895 Yale Station, New Haven.

**DELAWARE:** Dover, July 11-13. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

**DISTRICT OF COLUMBIA:** Basic Science. Washington, Dec. 26-27. Medical. Washington, Jan. 9-10. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

**GEORGIA:** Atlanta, June. Joint-Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

**IDaho:** Boise, April 4-7. Dir., Bureau of Occupational License, Mr. D. B. Cruikshank, Rm. 355, State Capitol Bldg., Boise.

**ILLINOIS:** Chicago, Jan. 24-26. Superintendent of Registration, Department of Registration and Education, Mr. Homer J. Byrd, Springfield.

**INDIANA:** Indianapolis, June 20-22. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

**IOWA:** Medical. Des Moines, Dec. 1-3. Basic Science. Des Moines, Jan. 10. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

**KANSAS:** Topeka, Dec. 13-14. Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 North 7th St., Kansas City.

**KENTUCKY:** Louisville, Dec. 6-8. Sec., State Board of Health, Dr. A. T. McCormack, 620 S. Third St., Louisville.

**LOUISIANA:** New Orleans, Dec. 1-3. Sec., Dr. Roy B. Harrison, 1507 Hibernia Bank Bldg., New Orleans.

**MARYLAND:** Medical (Regular). Baltimore, Dec. 13-16. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. Medical (Homeopathic). Baltimore, Dec. 13-14. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

**MICHIGAN:** Ann Arbor and Detroit, June 14-16. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 100 W. Allegan St., Lansing.

**MINNESOTA:** Basic Science. Minneapolis, Jan. 3-4. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. Medical. Minneapolis, Jan. 17-19. Sec., Dr. Julian F. DuBois, 350 St. Peter St., St. Paul.

**MISSISSIPPI:** Reciprocity. Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

**MONTANA:** Helena, April 4-5. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

**NEBRASKA:** Basic Science. Omaha, Jan. 10-11. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

**NEW HAMPSHIRE:** Concord, March 9-10. Sec., Board of Registration in Medicine, Dr. Fred E. Clow, State House, Concord.

**NEW JERSEY:** Trenton, June 20-21. Address, Dr. William L. Wilbur, 28 W. State St., Trenton.

**NEW MEXICO:** Santa Fe, April. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

**NEW YORK:** Albany, Buffalo, New York and Syracuse, Jan. 23-26. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, 315 Education Bldg., Albany.

**NORTH CAROLINA:** Reciprocity. Raleigh, December. Examination. Raleigh, June 19. Sec., Dr. William D. James, The Hamlet Hospital, Hamlet.

**NORTH DAKOTA:** Grand Forks, Jan. 3-6. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

**OHIO:** Columbus, Dec. 7-9. Sec., State Medical Board, Dr. H. M. Platter, 21 W. Broad St., Columbus.

**OKLAHOMA:** Basic Science. Oklahoma City, Nov. 30. Sec. of State, Hon. Frank C. Carter, State Capitol Bldg., Oklahoma City. Medical. Oklahoma City, Dec. 14. Sec., Dr. James D. Osborn Jr., Frederick.

**PENNSYLVANIA:** Philadelphia, Jan. 3-7. Sec., Board of Medical Education and Licensure, Dr. James A. Newpher, 400 Education Bldg., Harrisburg.

**PUERTO RICO:** San Juan, March 7. Sec., Dr. O. Costa Mandry, Department of Health, San Juan.

**SOUTH DAKOTA:** Pierre, Jan. 17-18. Director of Medical Licensure, Dr. B. A. Dyar, State Board of Health, Pierre.

**VERMONT:** Burlington, Feb. 14. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

**VIRGINIA:** Richmond, Dec. 14-16. Sec., Dr. J. W. Preston, 30½ Franklin Road, Roanoke.

**WASHINGTON:** Basic Science. Seattle, Jan. 5-6. Medical. Seattle, Jan. 9-11. Dir., Department of Licenses, Mr. Harry C. Huse, Olympia.

**WISCONSIN:** Basic Science. Milwaukee, Dec. 3. Sec., Prof. Robert N. Bauer, 3414 W. Wisconsin Ave., Milwaukee. Medical. Madison, Jan. 10-14. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

**WYOMING:** Cheyenne, Feb. 6. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

#### NATIONAL BOARD OF MEDICAL EXAMINERS SPECIAL BOARDS

Examinations of the National Board of Medical Examiners and Special Boards were published in THE JOURNAL, Nov. 19, page 1955.

### Colorado October Endorsement Report

Dr. Harvey W. Snyder, secretary, Colorado State Board of Medical Examiners, reports twelve applicants licensed by endorsement at the meeting held in Denver, Oct. 4, 1938. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Endorsement Grad. of
College of Medical Evangelists.....	(1924)	California,
(1933) Florida, (1938) N. B. M. Ex.		
Northwestern University Medical School.....	(1933)	Nebraska,
(1936) Illinois		

Rush Medical College.....	(1922)	(1927)	Illinois
State University of Iowa College of ..			Iowa
Johns Hopkins University School of ..			Utah
University of Minnesota Medical School.....	(1924)		Minnesota
Jefferson Medical College of Philadelphia.....	(1927)		New Jersey
Medical College of Virginia.....	(1937)		Virginia

### Iowa June Examination

Mr. H. W. Grefe, director, Division of Licensure and Registration, reports the written examination held at Iowa City, June 7-9, 1938. The examination covered eight subjects and included 100 questions. An average of 75 per cent was required to pass. Eighty-eight candidates were examined, of whom seventy-eight passed and ten failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Arkansas School of Medicine.....	(1937)	84.4	88.3
Rush Medical College .....	(1936)	79.9	(1937) 91.1
State University of Iowa College of Medicine.....	(1936)		86.4
(1938)* 78.8, 79.1, 80, 80.1, 80.5, 80.8, 81, 81.5, 81.9, 81.9, 81.9, 82, 82.4, 82.5, 82.5, 82.5, 82.9, 83, 83.1, 83.3, 83.4, 83.5, 83.8, 83.9, 83.9, 84.6, 84.6, 84.8, 84.9, 85.1, 85.1, 85.1, 85.4, 85.8, 86.1, 86.3, 86.3, 86.4, 86.5, 86.6, 86.6, 86.8, 86.8, 86.9, 86.9, 87, 87, 87, 87.1, 87.3, 87.4, 87.4, 87.5, 87.5, 87.6, 88, 88, 88.1, 88.3, 88.6, 88.6, 89, 89.3, 89.6, 90, 91, 91.1, 91.6, 92.5, 92.6			
University of Oregon Medical School.....	(1936)		88.1
Queen's University Faculty of Medicine.....	(1936)		83.8

School	FAILED	Year Grad.
State University of Iowa College of Medicine.....	(1938, 10)	

Thirty-three physicians were licensed by reciprocity and three physicians were licensed by endorsement from July 1 through Oct. 1, 1938. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Northwestern University Medical School.....	(1936)		California,
(1925), (1936), (1937) Illinois			
Rush Medical College .....	(1922)		Illinois
School of Medicine of the Division of Biological Sciences .....	(1934)		Illinois
University of Illinois College of Medicine (1931), (1936, 3), (1937), (1938, 2) Illinois			
Indiana University School of Medicine.....	(1929)		Indiana
University of Kansas School of Medicine.....	(1936, 2)		Kansas
University of Louisville School of Medicine.....	(1934)		Kentucky
University of Michigan Medical School.....	(1927)		Michigan
University of Minnesota Medical School.....	(1935, 2), (1937, 2)		Minnesota
Washington University School of ..	(1917)		Missouri
Creighton University School of ..			Nebraska
Univ. of Nebraska College of ..			Nebraska
Temple University School of Medicine.....	(1940)		New York
McGill University Faculty of Medicine.....	(1933)		Minnesota
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin	(1933)		New York
Schlesische-Friedrich-Wilhelms-Universität Medizinische Fakultät, Breslau .....	(1934)		New York

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists.....	(1938) N. B. M. Ex.		
Harvard University Medical School.....	(1933) N. B. M. Ex.		
Temple University School of Medicine.....	(1935) N. B. M. Ex.		

\* Licenses withheld pending completion of internship.

### California Reciprocity and Endorsement Report

Dr. Charles B. Pinkham, secretary, California State Board of Medical Examiners, reports fifty-one physicians licensed by reciprocity and twelve physicians licensed by endorsement from May 11 through Sept. 29, 1938. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
George Washington University School of Medicine.....	(1936)		Illinois
University of Georgia School of Medicine.....	(1937)		Georgia
College of Physicians and Surgeons of Chicago.....	(1910)		Illinois
(1912) South Dakota			
Rush Medical College.....	(1912)		Illinois
University of Illinois College of Medicine.....	(1936)		Illinois
State University of Iowa College of Medicine.....	(1911)		Iowa,
(1930) Utah			
University of Kansas School of Medicine.....	(1935)		Kansas
University of Louisville School of Medicine.....	(1934)		Kentucky
University of Minnesota Medical School.....	(1925)		Minnesota
Harvard University School of Medicine.....	(1926)		Mass.
..	(1928), (1930)		Michigan
..	(1928)		Montana
..	(1928)		Idaho
..	(1928)		Missouri
..	(1928)		Oregon,
..	(1928)		
Creighton University School of Medicine.....	(1937)		Kansas
John A. Creighton Medical College .....	(1902)		Illinois
University of Nebraska College of Medicine.....	(1928)		Hawaii,
(1933) New York, (1908), (1917), (1932, 2), (1934, 2), (1937, 2) Nebraska			
Columbia Univ. College of Physicians and Surgeons.....	(1928)		New York

Eclectic Medical College of the City of New York....	(1901)	New York
New York University, University and Bellevue Hos- pital Medical College.....	(1917), (1928)	New York
University of Buffalo School of Medicine.....	(1900)	New York
University of Rochester School of Medicine.....	(1934)	New York
University of Cincinnati College of Medicine.....	(1938)	Ohio
Western Reserve University School of Med....	(1936), (1937)	Ohio
University of Oregon Medical School.....	(1936)	Oregon
Jefferson Medical College of Philadelphia.....	(1909)	Minnesota
(1924) Pennsylvania, (1934) Ohio		
University of Pennsylvania School of Medicine.....	(1924)	New York
Woman's Medical College of Pennsylvania.....	(1915)	New York
University of Vermont College of Medicine.....	(1923)	Vermont
University of Virginia Department of Medicine.....	(1932)	Virginia
University of St. Andrews Conjoint Medical School, Scotland .....	(1934)	New York
SCHOOL		
LICENSED BY ENDORSEMENT		
College of Medical Evangelists.....	(1936)	N. B. M. Ex.
University of Colorado School of Medicine.....	(1931)	U. S. Navy
Tulane University of Louisiana School of Medicine.....	(1931)	N. B. M. Ex.
Harvard University Medical School.....	(1934)	N. B. M. Ex.
St. Louis University School of Medicine.....	(1930), (1933)	N. B. M. Ex.
New York University, University and Bellevue Hos- pital Medical College.....	(1927)	N. B. M. Ex.
University of Rochester School of Medicine.....	(1935)	N. B. M. Ex.
Duke University School of Medicine.....	(1934, 2)	N. B. M. Ex.
University of Oregon Medical School.....	(1929)	N. B. M. Ex.
University of Pennsylvania Department of Medicine..	(1898)	U. S. Army

## Book Notices

**Experience in the Management of Fractures and Dislocations (Based on an Analysis of 4,390 Cases).** By the Staff of the Fracture Service, Massachusetts General Hospital, Boston. Under the General Editorship of Philip D. Wilson, M.D., Surgeon-in-Chief, Hospital for Ruptured and Crippled, New York. Cloth. Price, \$15. Pp. 1,036, with 1,419 illustrations. Philadelphia, London & Montreal: J. B. Lippincott Company, 1938.

The staff of the Fracture Service of the Massachusetts General Hospital in Boston presents in this book a study of 3,985 patients who suffered 4,390 fractures and dislocations. Of this number they obtained end result examinations, a year or more after injury, in 1,192 cases. Their unusual presentation includes summaries of the history, examination, treatment and final examinations for each one of these end result cases, and also, for most of them, tracings of the early to late x-ray films. The twenty-three collaborators summarize the injuries in the various regions of the body. Following the introduction is the chapter on fractures and dislocations of the phalanges and metacarpals, which includes forty-five brief case histories outlining the associated injuries, treatment, complications and end results, and adjacent to this summary are sketches of the x-ray films in practically all the cases. Then follows the chapter on fractures and dislocations of the carpal bones by another member of the staff, with a brief introductory discussion of the anatomic considerations and a general consideration of the material studied. This chapter is concluded by summaries of twenty-six case histories, mostly accompanied by the pictures in each case. That is the general plan of presentation, which continues through the book. Chapter XVII is entitled "Fractures of the Facial Bones"; chapter XV, "Fractures and Dislocations of the Cervical Spine"; chapter XI, "Dislocation of the Shoulder Girdle"; chapter XIX, "Fractures of the Pelvis"; chapter XXII, "Ankle Fractures"; chapter XXXI, "Pathologic Fractures"; chapter XXXIII, "Delayed and Nonunion," and so on. The summaries of case reports are set in different type from the text. They begin with case report 1 in chapter II and end with case report 1396 in chapter XXXI.

This presentation differs from other treatises on fractures in that it is based on the actual study of cases and the analysis of the results of treatment. The authors have not gleaned all the information that may be obtained from analysis of these cases, and this large amount of source material is placed at the disposition of any student who cares to search further in the desire that every worthwhile conclusion may be drawn.

With the toll of injured victims ever increasing, physicians are confronted daily with problems on the correct solutions of which depend human lives. Conscious of such responsibility, practitioners are attending graduate fracture courses in ever increasing numbers.

The staff of the Fracture Service of the Massachusetts General Hospital for many years has conducted annually a graduate course on fractures. This book is the outgrowth of their teaching. The authors of the various chapters are those who

have taught in these courses in the field in which they were particularly competent. They are conscious of defects in this presentation, but the sincerity of their figures cannot be questioned. They have reported fully the unsatisfactory results along with the good results. Some of the bad results, however, were inevitable from the nature of the injury, and some of them were due to errors of judgment or mistakes in technic. The authors hope that this presentation may challenge others to present similarly their material. When a large body of facts representing results of treatment by all the different methods are available for study, progress will follow.

**A Handbook of Methods for the Study of Adolescent Children.** By William Walter Greulich, Ph.D., Harry G. Day, Sc.D., Sander E. Lachman, M.D., John B. Wolfe, Ph.D., and Frank K. Shuttleworth, Ph.D. Monographs of the Society for Research in Child Development, Volume III, No. 2 (Serial No. 15). Paper. Price, \$2.25. Pp. 406, with 30 illustrations and diagrams. Washington, D. C.: Society for Research in Child Development, National Research Council, 1938.

**The Adolescent Period: A Graphic and Pictorial Atlas.** By Frank K. Shuttleworth, Institute of Human Relations, Yale University, New Haven, Conn. Monographs of the Society for Research in Child Development, Volume III, No. 3 (Serial No. 16). Paper. Price, \$2. Pp. 246, with 458 illustrations and graphs. Washington, D. C.: Society for Research in Child Development, National Research Council, 1938.

The handbook and atlas have been prepared by a group of scientists who, over an appreciable period, have jointly reviewed critically and examined the literature on adolescence. Lawrence K. Frank, in an introduction, explains that the handbook is intended to be a methodological aid for students of child growth and development, particularly of the adolescent period. The several authors have covered the particular fields of their specialized interest. The material is organized in five parts, anatomic studies, biochemical and physiologic researches, medical and clinical aspects of adolescence, psychologic investigations, and a section on problems not involving direct measurements of children. The effort has been "to select from the literature those methods, technics and procedures which might be employed to record and, if possible, measure the growing child, in order to reveal the rate and direction of growth and development, or the developmental sequence, of the various structures, functions and activities that are being observed" (xv).

In the section on anthropometry, Dr. Greulich characterizes serial photography as the most valuable single technic for recording externally discernible bodily changes associated with growth and development. The general physical characteristics and changes associated with puberty are outlined extensively. The section on biochemical and physiologic aspects exhaustively covers the literature of the physiology of the skin, blood chemistry, respiration and energy metabolism, digestive organs, urine and feces. The extensive psychologic section comprehensively covers the literature on sensory and motor phenomena, intellectual and educational achievement and special abilities. The literature on sexual behavior is briefly and critically commented on to the effect that "but little in the way of established facts or well tried methods of obtaining facts" on adolescent sexual behavior is to be found. Much more exhaustive review of tests and observations of personal and social reactions is given. A final section presents literature on measurable aspects of the environment, discusses the logic of the approaches to the heredity-environment problem, and concludes with a discussion of statistical considerations.

The separate monograph, the atlas by Dr. Shuttleworth, consists of illustrations presenting data concerning adolescents and adolescent growth. They include graphs, charts, diagrams, photographs and all manner of data suitable for graphic or pictorial presentation. Material has been presented from the many aspects from which the adolescent is studied, physical growth and development, sexual maturation, health statistics, intellectual development, problems of behavior and occupational and sexual adjustments.

These two related works constitute a monumental achievement in selection and (in the handbook) of critical discussion of contributions from a vast and often confusing literature, which they now bring within relatively easy reach of the student or research worker. As a reference resource they amply justify the enormous labor they represent. As the authors have set out to do, they indicate what structures, functions and

activities of the growing child can and have been measured, and they aid the worker in making reliable measurements of his own.

Despite its bigness, the handbook omits the neurologic, psychiatric and endocrinologic literature of adolescence, which omission, the authors explain, is due to limitations of time and personnel. From the standpoint of the medical research worker in adolescence this is a disappointing omission, and the authors' hope that others will be inspired to make up for this lack will be shared by medical workers. One cannot lightly dismiss, however, the almost cursory manner in which some relatively subjective methods of studying behavior are dismissed in chapter XXI. These include observation, personal report (interviews, psychoanalysis, case study) as discussed in the chapter on sexual behavior. These methods should be critically regarded as methods of study of behavior in general, sexual or otherwise. The possibilities of these methods are sufficiently great that serious students of behavior should not content themselves with the easy evasion "as the procedure (psychoanalysis) now stands, however, it appears to be too subjective to be classified as a scientific approach." The authors make tentative suggestions as to the possible "scientific" utilization of these methods. They persist in the curious attitude that methods which gain information about the mental life of the disturbed individual might not be useful in gaining information about the normal adolescent. According to this logic, study of an individual suffering with an infection might not be expected to throw light on the maintaining of immunity from disease by the normal individual who shows no sign of infection. Not infrequently it requires the observation of individuals presenting exaggerated reaction to undue stress (whether physical or psychologic) to suggest the reactive potentialities and the laws governing these for the normal individual. Observation, whether of individuals in health or in disease, may lead to the clues necessary to set up properly controlled conditions for scientific investigation. (See D. M. Levy, *Studies in Sibling Rivalry*, American Orthopsychiatric Association, 1937, as an attempt in this direction.)

One would judge that after their experience in sifting such an immense literature the authors might be in a position to influence somewhat the direction of experimentation and observation that may tend toward a clearer conception of the adolescent, who still seems lost in the woods. If so, this may be reflected in the literature on adolescence of the next few years. Workers in the field of child development who will trouble to make proper use of these two publications will gain much profit for their pains.

*Some Account of the Pennsylvania Hospital from Its First Rise to the Beginning of the Year 1938.* By Francis R. Packard, M.D. Boards. Price, \$2.50. Pp. 133, with 44 illustrations. Philadelphia: Pennsylvania Hospital, 1938.

Firsts in various fields, whether books or buildings, are interesting. It is also important for American men of medicine to know something about the first hospital in the United States. This brief work by Packard, who is exceptionally well qualified as a medical historian, is full of important items. Benjamin Franklin while a member of the board of the Pennsylvania Hospital prepared and printed in his own printing plant a history of the hospital. To add to its historic value, "in the making of the present volume the printers have followed in general the size, format and typography of the earlier work." The Pennsylvania Hospital was founded in 1751. To quote from chapter II of Dr. Packard's work, "one of the objections made to the foundation of the hospital, when the matter was first brought up in the assembly, had been the expense that would be incurred in securing the services of physicians and surgeons for its staff. This was obviated when Drs. Lloyd Zachary, Thomas Bond and his brother, Phineas Bond, offered not only to serve the hospital for three years without compensation but also to supply all the medicines for that time at their own expense." What a fine commentary this is on the character of those men, and how timely it is to call attention to the fact that the medical profession at all times has served the best interests of humanity. The development of many departments and innovations is mentioned. Among these were the laboratory, first used as a place to

prepare drugs for the hospital. Then a sunstroke tent was erected, consisting of a large canvas pavilion, as a temporary but useful annex to the hospital, which served for some years and in which Dr. James J. Leveck introduced the so-called ice treatment for sunstroke. Although the Pennsylvania Hospital was founded largely by the Quakers and their influence, nevertheless it is "the only hospital in this country that has cared for sick or wounded soldiers in all the wars which have occurred on its soil." The staff of the hospital was a most distinguished one and the "high standard set by the original staff was well maintained in subsequent years." According to the author it was in the operating room of the Pennsylvania Hospital that the first thoracoplasty in a case of pulmonary tuberculosis was performed Nov. 13, 1911, by Dr. R. G. Le Conte. This brief work is embellished with a goodly number of interesting illustrations and presents at its close an iconography listing the various authorized engravings of the hospital. Dr. Packard's charming style makes this a delightful production from a literary standpoint. It is also most valuable as a historical document, one which lovers of medicine and those interested in its development in Philadelphia should read and thereby be both instructed and edified.

*Medicina legal y criminología afrocubanas.* Por Israel Castellanos, director del Gabinete nacional de Identificación de la República de Cuba. Paper. Pp. 152, with 26 illustrations. Havana: Molina y Cla, Impresores, 1937.

The study of medicolegal problems involved in medicine as practiced by the Cuban-African Negro witch doctor is of considerable sociologic interest and importance. The native physician sorcerers have, in their own circle, the right to kill as well as the right to cure. These sorcerers, called *ninigos* and *Brujos*, have often been referred to as criminals and yet in their social structure they are the omnipotent guardians of their race. Perhaps the most comprehensive study of the customs of these sorcerers is the book by Fernando Ortiz. The volume by Castellanos is not nearly as complete as the one by Ortiz but does give an insight into the medicolegal aspect of this problem, which is far from being solved.

*The Principles and Practice of Obstetrics.* By Joseph B. DeLee, A.M., M.D., Consultant in Obstetrics, Chicago Lying-in Hospital and Dispensary, Chicago. Seventh edition. Cloth. Price, \$12. Pp. 1,211, with 1,277 illustrations. Philadelphia & London: W. B. Saunders Company, 1938.

This book has now been before the profession for twenty-five years. It still reflects the teachings of the well known author at Northwestern University Medical School and at the University of Chicago. The obstetric technic described is the result of his experience of forty-four years in many hospitals, in a large maternity outdepartment, and in private and consulting practice in many homes. He has carefully worked over this new edition, adding much new material and omitting some obsolete material. The book remains virtually the same size as the preceding edition. Rapid developments in the physiology of menstruation and in the blood chemistry of the toxemias of pregnancy made necessary considerable revision of those sections in which work the author was assisted by Profs. M. E. Davis, W. J. Dieckmann and G. M. Dack of the University of Chicago. Dr. DeLee believes that lack of knowledge of the natural phenomena in labor is responsible for much of the present high maternal and fetal mortality. He has given therefore special attention to the mechanism of labor, incorporating the great contributions made by Caldwell, Moloy and D'Esopo, Rudolph and Ivy, and de Snoo. The chapter on obstetric anesthesia and analgesia has been enlarged. While nature intended labor to be a simple and harmless function, the softening influences of modern life, the author believes, have something to do with the present day suffering during childbirth. Nevertheless, the author has seen three painless labors and many others in which the pains were easily bearable, until at the very finish a few whiffs of ether completed a satisfactory delivery. The pain of labor, he believes, has been much exaggerated and attempts to get rid of all of it have been dangerous. In this chapter he discusses various anesthetics that have been used to relieve the pain of labor.

The chapter on contracted pelvis may seem long to those practitioners who do not make pelvic measurements or an antepartum study of the probable mechanism of labor. There is

much to learn about contracted pelvis and nature's method of overcoming mechanical difficulties. The developments in the endocrine or vitamin fields which appear to have been proved useful, the developments in internal medicine and surgery in their relation to pregnancy and tuberculosis, heart disease, diabetes and the anemias, have been incorporated as well as the treatment of puerperal sepsis by means of sulfanilamide and the new scalp traction forceps in placenta praevia. The author has kept the text representative of the obstetric thought of the day and his book remains preeminent in this field.

*Les méningo-neurobrucelloses.* Par Henri Roger et Yves Poursines. Paper. Price, 45 francs. Pp. 248. Paris: Masson & Cie, 1938.

Until recently, scant attention has been paid to the influence of brucellosis (undulant fever) on the central or peripheral nervous system. While scattered reports have appeared in American medical literature describing cases of meningitis or encephalitis due to *Brucella* infection, the attention of American physicians has not been directed particularly toward the frequency of those complications of brucellosis which affect the nervous system. Especially during the past decade, many reports have appeared in European literature, particularly in French journals, dealing with the neurobrucelloses. Roger and Poursines have brought together a combined account of their own researches and the published observations of other workers. The result is a masterly dissertation which deals concisely and clearly with an undoubtedly common, but infrequently recognized, phase of brucellosis. The predilection for meningeal localization, frequently associated with involvement of other parts of the nervous system, caused Roger and Poursines to select the descriptive name "meningoneurobrucellosis." The authors provide convincing evidence that the role of the meningitis predominates and that other nervous system involvement is usually secondary to the meningitis. Emphasis is placed on the long interval, often months or years, which may intervene between the acute phase of brucellosis and the delayed manifestations of neuromeningeal complications. The clinical manifestations vary greatly, depending on the extent of meningeal involvement and the presence of additional complications involving the brain, spinal cord or peripheral nerves. Not infrequently the symptoms simulate those of tuberculous meningitis, cerebrospinal syphilis or spinal cord tumor. The diagnostic, prognostic and therapeutic considerations are discussed in an adequate manner. This book should serve a useful purpose in stimulating physicians, particularly neurologists, to consider brucellosis as a not infrequent etiologic factor in many varieties of disease of the nervous system.

*The Rheumatic Diseases: A Course of Lectures Arranged by the Medical Staff of the St. John Clinic and Institute of Physical Medicine.* Edited by Sir Leonard Hill, M.B., LL.D., F.R.S., Director of Research, St. John Clinic and Institute of Physical Medicine, and Philip Ellman, M.D., M.R.C.P., Physician to St. John Clinic and Institute of Physical Medicine, London. With a foreword by Sir Arthur MacNalty, K.C.B., M.D., F.R.C.P., Chief Medical Officer to the Ministry of Health. Cloth. Price, \$4. Pp. 270, with 46 illustrations. Baltimore: William Wood & Company, 1938.

The editors of this book have assembled a course of lectures on rheumatic disease which had been given by members of the staff of the St. John Clinic and Institute of Physical Medicine and authorities from elsewhere during the winter and spring of 1936-1937. There are fifteen contributors and the result is a volume which, while lacking in integration and in the careful editing of some chapters, furnishes a number of thought provoking views. The chapter by R. Fortescue Fox is especially stimulating. His emphasis on the individual nature rather than the purely statistical position of the man of 35 or the young housewife with children faced with a life of progressive crippling deserves constant repetition. Furthermore, his discussion of the known incidence and economic cost of rheumatic disorders in several European countries throws into sharp contrast the almost complete lack of accurate information available in the United States. Fox's discussion also illustrates the greater extent of facilities for the care of chronic arthritis in some European countries, especially Sweden, which nearly twenty years ago erected three sanatoriums for physical, mental and occupational treatment. There is some difference of opinion expressed by the various authors, as was in fact intended, the "unitary theory" of rheumatic fever and rheumatoid arthritis

being supported by Sir William Wilcox and others, while Professor Leonard Findlay contends that the evidence in favor of the "unitary theory" is unconvincing. In the chapter by Koerner and Poulton, "Antistreptolysins and Blood Uric Acid in the Chronic Rheumatic Diseases," some original work is reported. Among other conclusions they found that the value of prontosil and prontosil album in rheumatoid arthritis is doubtful except perhaps in the more acute cases. Five chapters are devoted to problems of physical medicine in relation to rheumatic disease. The lecture by H. J. Taylor on the physical basis of physical medicine should serve as a worthwhile introduction to the subject especially for those whose memory of physics has faded. While there may be some difference of opinion with regard to the indications and effectiveness of the various types of physical therapy, these chapters are valuable in expressing the views of experienced workers.

*Aids to Histology.* By Alexander Goodall, M.D., F.R.C.P., Lecturer on Physiology, School of Medicine of the Royal Colleges, Edinburgh. Fourth edition. Cloth. Price, \$1.25. Pp. 151, with 26 illustrations. Baltimore: William Wood & Company, 1938.

This pocket-sized volume is an attempt to present the essential facts of histology in brief form. The author believes that the apparent complexity of histologic structure with the large number of technical terms bewilders the beginner and that a short guide may be of more service to junior students than lengthy descriptions. The book begins with a definition of histology, which word comes from *histos*, meaning a web. Brief discussions follow on the cell, mitosis and the ovum. Following is a five page chapter on epithelium. The next chapter takes up the connective tissues, the reticulo-endothelial system and the different kinds of cartilage. There is a three page chapter on muscle, and there are numerous brief chapters on various other systems. The nervous system is treated more fully. There are not many illustrations. This volume no doubt would aid in simplifying the extended discussions found in textbooks on histology. The book has gone into four editions since 1911.

*What's Wrong With Me?* By H. Ameroy Hartwell, M.D. Cloth. Price, \$1. Pp. 246. Weehawken, N. J.: The Author, 1938.

This book must be regarded as fundamentally unjustifiable and in violation of one of the most important established truths relating to health. It consists of a series of semitabular statements of symptoms, from which the patient is supposed to make his own tentative diagnosis, then go to a doctor for verification by the objective physical signs, and to seek the physician for treatment. The list of diseases dealt with starts with "abortion" and goes on through the alphabet to "yellow fever." It includes such serious conditions as acute appendicitis, acute Bright's disease and acute gastritis; these, incidentally, alphabetized under "acute." The book can be of little service to the layman and may result in raising needless alarms and contributing to the development of neuroses, unfounded fears, delay in correct diagnosis and treatment or hypochondriasis.

*Die Diffusionsanalyse am Blutplasmagel: Ein neuer Weg der Blutforschung.* Von Rudolf Bucher. Paper. Price, 30 Swiss francs. Pp. 123, with 70 illustrations. Basel: Benno Schwabe & Co., 1937.

This is a highly technical monograph describing original experiments applying the Liesegang ring phenomena to blood plasma. The author claims to have found certain specific differences in plasma from various species. He observed a characteristic pattern shift with age in all species, and certain changes in disease. These phenomena are apparently independent of total protein concentration. Their interpretation is obscure. The characteristic patterns are illustrated by excellent color plates.

*Materia Medica, Drug Administration and Prescription Writing.* By Oscar W. Bethea, M.D., Ph.G., Ph.M., Professor of Clinical Medicine, Tulane School of Medicine, New Orleans, La. Fifth edition. Cloth. Price, \$5. Pp. 577. Philadelphia: F. A. Davis Company, 1938.

In this book, which long ago established a place for itself, the reader finds a compendium of the drugs of the U. S. Pharmacopeia XI and the National Formulary VI, together with an excellent treatise on prescription writing. Not only are the drugs described but there are also historical sketches of many of the more important ones, and numerous prescriptions (properly credited to the standard works on therapeutics from



which they are drawn) are offered to illustrate the chief methods of their employment. The revision for the fifth edition has apparently been thorough and will certainly justify for the book a continued occupancy of one of the leading places in this textbook field.

**Attaining Manhood: A Doctor Talks to Boys About Sex.** By George W. Corner, M.D., Professor of Anatomy, the University of Rochester, Rochester, N. Y. Cloth. Price, \$1.25. Pp. 65, with 15 illustrations. New York & London: Harper & Brothers, 1938.

This is an excellent brief discussion of sex for adolescent boys. It avoids sensationalism and gives all the necessary information in condensed form. The diagrams of the sex organs of both the male and the female are exceptionally clear. The book is characterized by a strikingly unemotional style. Its brevity also commends it. The physician who seeks a book to recommend for growing boys, either his own or those of his patients, will make no mistake in choosing this one.

## Bureau of Legal Medicine and Legislation

### MEDICOLEGAL ABSTRACTS

**Workmen's Compensation Acts: Refusal to Undergo Third Operation for Hernia.**—Lindley, in the course of his employment, sustained an injury which resulted in double inguinal hernias. He submitted to two successive operations to correct the hernia on his left side but both operations proved unsuccessful. He then refused to submit either to a further operation to repair the condition on his left side or to an operation for the hernia on his right side. In proceedings instituted under the Oklahoma workmen's compensation act he was awarded compensation for permanent total disability and the employer appealed to the Supreme Court of Oklahoma.

Lindley's disability seemed to be due solely to his left inguinal hernia. The medical testimony on his behalf was to the effect that, because of his condition and the scar tissue which had formed as a result of the previous operations, further surgery was contraindicated and would be attended with more than usual danger and risk to health and life. While the employer's medical testimony tended to minimize the danger incident to a third operation, all the medical testimony was in substantial agreement that the presence of scar tissue would make the success of a further operation more problematic than it would otherwise be; that Lindley's disability would be permanent unless relieved by an operation; and that so long as the condition was unrelieved the performance of heavy manual labor would constitute a constant threat to health and life. While, said the court, no award can be made for permanent disability for hernia until the workman has submitted to an operation to correct the condition, a workman who has undergone such an operation and has received no relief therefrom is not thereafter required to submit to further operations on the chance that they may prove successful. This rule was announced in *United Service Street Car Co. v. McCarter*, 167 Okla. 433, 30 P. (2d) 456, in the following language:

An injured workman who is permanently and totally disabled by reason of a recurring hernia, and who has undergone one unsuccessful operation, is not required to subject himself to another operation which would be dangerous and probably useless, in order to minimize the financial burden imposed by law on his employer or his employer's insurance carrier.

The employer contended, furthermore, that Lindley had not sustained a permanent total disability as a result of the hernias, because the evidence showed that he actually performed work of substantially the same kind and character after his injury as he had performed prior thereto. With respect to this contention, Lindley testified that he had continued his work as a matter of necessity to provide for himself and for his wife and children. Ordinarily, said the Supreme Court, a disability cannot be classified as total under the workmen's compensation act where the earning power of the workman is not wholly destroyed and capacity to perform remunerative employment remains. Excluded from this rule, however, are those cases in which the

capacity of the workman is confined to the performance of work of a slight or trivial nature and those cases in which the capacity to do ordinary manual labor remains, as in the present case, but can be exercised only at the cost of serious discomfort and pain on the part of the workman. Sometimes men are impelled by stark necessity or a strong sense of duty and obligation to labor and to seek to carry on long after the human machine has been so broken and destroyed as to seem to make it impossible to drive it further. The wisdom of the effort and the struggle under such conditions may be questioned but the gallantry of the action should not be penalized. The evidence before the commission showed that Lindley had carried on under the urge of necessity and that in so doing he had risked both his health and his life and that the disability under which he was laboring would probably be permanent. Under such circumstances, said the Supreme Court, the commission was justified in finding that Lindley had sustained a permanent total disability as a result of his industrial injury. The court accordingly affirmed the award of compensation.—*Dierks Lumber & Coal Co. v. Lindley (Okla.)*, 77 P. (2d) 44.

**Workmen's Compensation Acts: Lead Poisoning as a Compensable Injury.**—Burden worked in an automobile assembly line near other workers who were grinding down rough spots on metal automobile bodies which had been treated with a lead compound. The air in this part of the plant was impregnated with lead dust and fine metal filings. On March 10, 1936, another worker, in using a compressed air hose, unexpectedly blew a cloud of lead dust into Burden's eyes, nose and mouth. About a week later he began to suffer from headaches, pains about his body, and cramps in his joints; his gums became tender and painful; urination was frequent and painful; and he suffered from nervousness and sleeplessness. As a result he was forced to quit work April 3, 1936. In May his condition was diagnosed as lead poisoning. He applied for and was granted compensation under the Texas workmen's compensation act and his employer's insurer filed an action in the appropriate federal district court to vacate the industrial board's award. From an adverse judgment by the district court, the insurer appealed to the United States circuit court of appeals, fifth circuit.

The insurer contended that Burden's condition was the result of an occupational disease and hence not compensable under the Texas act. Clearly, said the circuit court of appeals, Burden was disabled from lead poisoning. If this were solely the result of a gradual absorption of lead dust as a natural and ordinary hazard of his employment, it would not be compensable. There was evidence, however, of an unexpected, unintended and forcible blowing of an unusually large quantity of lead dust into Burden's face, nostrils and mouth about March 10, 1936, from which it may be found that he then accidentally inhaled an abnormal quantity. There was medical testimony to the effect that the gradual absorption of lead over a period of years would render a person less tolerant to lead than normally, and consequently more susceptible to a massive dose suddenly received; that "the amount of lead he had absorbed over the course of several years would be deposited into the bones and tissues, and probably would not have given any distress, unless he had a large dose to cause acute symptoms"; and that, if he had not had this lead in his system by this constant everyday absorption over four years of time, a massive dose would have caused a disability at the time anyway. The evidence was ample, in the opinion of the court, to support a finding of a compensable industrial injury.

The failure of Burden, in violation of a rule of employment, to wear a respirator which was provided for him and which presumably would have prevented his inhaling the lead dust did not defeat his claim for compensation, continued the court. When a workman is injured while doing something he is not employed to do—an act which is itself outside the scope of his employment—such injury is generally held not compensable because not suffered in the course of employment. Where, however, as here, the workman merely violates a rule relating only to the manner and method of doing his own work, such a violation does not defeat his right to compensation.

The award of compensation in favor of the workman was accordingly affirmed.—*Travelers Ins. Co. v. Burden*, 94 F. (2d) 880.

## Society Proceedings

### COMING MEETINGS

American Academy of Orthopedic Surgeons, Memphis, Tenn., Jan. 15-19. Dr. Carl E. Badgley, 1313 East Ann St., Ann Arbor, Mich., Secretary.  
American Association for the Study of Neoplastic Diseases, Baltimore, Dec. 28-30. Dr. Eugene R. Whitmore, 2139 Wyoming Avenue N.W., Washington, D. C., Secretary.  
American Student Health Association, New York, Dec. 29-30. Dr. Ruth E. Boynton, Students Health Service, University of Minnesota, Minneapolis, Secretary.  
Eastern Section, American Laryngological, Rhinological and Otolological Society, Boston, Jan. 11. Dr. Frank E. Kittredge, Masonic Temple, Nashua, N. H., Chairman.  
Middle Section, American Laryngological, Rhinological and Otolological Society, Sioux City, Iowa, Jan. 19-20. T. R. Gittins, Davidson Bldg., Sioux City, Iowa, Chairman.  
Pacific Coast Society of Obstetrics and Gynecology, Los Angeles, Nov. 30-Dec. 3. Dr. T. Floyd Bell, 400 29th St., Oakland, Calif., Secretary.  
Radiological Society of North America, Pittsburgh, Nov. 28-Dec. 2. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y., Secretary.  
Society for the Study of Asthma and Allied Conditions, New York, Dec. 3. Dr. W. C. Spain, 116 East 53d St., New York, Secretary.  
Southern Section, American Laryngological, Rhinological and Otolological Society, New Orleans, Jan. 14. Dr. Francis E. LeJeune, Maison Blanche, New Orleans, Chairman.  
Southern Surgical Association, White Sulphur Springs, W. Va., Dec. 6-8. Dr. Alton Ochsner, 1430 Tulane Ave., New Orleans, Secretary.  
Western Surgical Association, Omaha, Dec. 2-3. Dr. Albert H. Montgomery, 122 South Michigan Blvd., Chicago, Secretary.

### THE AMERICAN RHEUMATISM ASSOCIATION

*Fifth Annual Meeting and Seventh Conference on Rheumatic Diseases, held in San Francisco, June 13, 1938*

LORING T. SWAIM, M.D., Boston, Secretary

(Continued from page 1962)

#### Immunologic and Bacteriologic Observations in Experimental Streptococcic Arthritis

DRS. D. MURRAY ANGEVINE, RUSSELL L. CECIL and SIDNEY ROTHBARD, New York: During a study of infectious arthritis in rabbits it was found that a small amount (from 0.1 to 2 cc.) of a broth culture of hemolytic streptococcus (AB 13) when injected intravenously produced arthritis in 87 per cent of fifty-four animals. The sedimentation rate was increased and streptococcic agglutinins were demonstrated in those animals which developed arthritis as well as in those which failed to do so. Cutaneous tests were done frequently, and only about 50 per cent of the rabbits developed sensitivity to streptococcus filtrate. Experiments were performed to determine whether there were any differences in the arthritis in normal and in immunized rabbits. Two groups of ten rabbits each received repeated injections of heat-killed organisms. One group was injected intradermally and the other intravenously. The intradermally immunized group became highly sensitive and the intravenously immunized group only slightly sensitive to intradermal injections of streptococcus filtrate. The immunized animals together with a group of normal rabbits were injected intravenously with 2 cc. of a broth culture of hemolytic streptococci. There were no conspicuous differences in the time of onset, the number of joints involved, the severity or the microscopic picture of the arthritis that developed in the three groups of animals. This experiment was repeated, but the rabbits were infected with multiple and varying doses. The first dose was 0.1 cc. of culture injected intravenously; ten days later 1 cc. was given and ten days after this 2 cc. Five of the nine intravenously immunized rabbits developed arthritis after the first infecting dose of 0.1 cc., whereas only one of eight intradermally immunized rabbits and two of eleven controls developed arthritis. Considerably less arthritis was found in this group at the time of necropsy than in the normal and intradermally immunized rabbits. This experiment indicates that although intravenous immunization caused a slight increase in susceptibility to arthritis there was also some protection against the development of arthritis.

#### DISCUSSION

DR. M. HENRY DAWSON, New York: These experiments clearly show that it is possible to produce a nonsuppurative arthritis in rabbits by the intravenous injection of small doses of hemolytic streptococci. The authors have shown that it is

possible to produce lesions which pathologically resemble closely those found in rheumatoid arthritis. However, the disease which they have experimentally produced differs in certain essential respects from the naturally occurring disease and no claims whatever are made that they have reproduced rheumatoid arthritis. There are two points in which the experimental disease differs from the naturally occurring one: In the experimental disease both the agglutinins and the sedimentation rate quickly return to normal. In rheumatoid arthritis the agglutinins persist throughout the disease and the sedimentation rate returns to normal only when the process becomes quiescent. Two other points are worthy of comment. The first is that normal rabbits, immune rabbits and hypersensitive rabbits were all found to respond in essentially the same manner. This is an important observation and should cause much concern to those who believe in allergic theories as well as those who believe in the value of vaccine therapy. The second point concerns the similarity in the agglutination results in the experimentally infected rabbits and in the natural disease rheumatoid arthritis. For many years I have been deeply interested in the capacity of rheumatoid arthritis serums to agglutinate hemolytic streptococci of group A. However, I have always been a little disturbed by the fact that this property is present in only about 70 per cent of cases. From the results reported today it would appear that agglutinins are similarly present in only 70 or 80 per cent of infected animals. It may well be that the failure of the remainder to respond may be associated with the feeble antigenic properties possessed by group A organisms.

DR. J. ALBERT KEY, St. Louis: I believe that in the beginning these streptococcic joints were purulent, but they are undoubtedly the nearest approach to experimental rheumatoid arthritis that I have seen. I have seen acute streptococcic joints in patients which quiet down and produce a chronic progressive arthritis. Usually, however, this is of a destructive character. In my experience, once the acute stage of the experimental infection was over there were no further involved joints. This is one of the distinguishing features between rheumatoid arthritis and experimental streptococcic arthritis. In my experimental arthritis I produce an acute arthritis in certain joints and there are no more joints involved. Clinically, unfortunately, that doesn't happen. The results of immunization were similar to my experience a few years ago. In a group of animals I tried to sensitize some and immunize others. I then injected small doses of streptococci directly into the joints. Streptococcus viridans and hemolytic streptococci were used and in all instances I was able to produce a purulent arthritis, regardless of whether or not the rabbits had been immunized or sensitized or were controls. In other words, I was not able to detect any difference between the three groups of animals. I have never accepted Ghormley and Allison's statement that there is a specific microscopic picture for atrophic arthritis. Joint tissues can react only in certain ways and if one submits the joint to a long drawn out chronic infection one gets proliferative changes and round cell infiltration and one may find these round cells in nodules with a relatively clear center. This microscopic picture can be produced in different ways and it is the result of chronic inflammation rather than of a specific type of infection.

DR. JAMES F. RINEHART, San Francisco: I am inclined to agree with Dr. Key that the experimental arthritis of Dr. Angevine and his co-workers may have been suppurative at the onset. At least it has not been clearly shown that this was not so. The chronic scorbutic arthritis in guinea pigs is distinctly a polyarthritis. If the deficiency is maintained over a period of time, various joints are involved in sequence. The knee joints usually are first affected and subsequently the wrists, the elbows and other joints. The arthritis is of a proliferative type. I would like to echo Dr. Key's remark about specificity of certain pathologic changes in rheumatoid arthritis. I do not believe that focal accumulations of lymphocytes in the subsynovial tissues can be considered specific for this type of arthritis. The subcutaneous nodule and comparable reactive changes in the periarticular tissues are probably much more nearly if not actually specific for this disease.

DR. D. MURRAY ANGEVINE, New York: When large doses of hemolytic streptococci are injected, the animals develop arthritis in practically every joint. In these cases the synovial fluid is usually purulent. However, if the dose is reduced so that the animal is not overwhelmed by the injection, an entirely different picture is seen in the joints. At first the process is an acute inflammatory one that is characterized by an increase in the number of polymorphonuclear leukocytes in the synovial fluid. However, this material is not frankly purulent and I do not believe that such a joint should be described as suppurative, although it would be regarded as an acute inflammatory exudate. When one does a necropsy on an animal with arthritis produced by a staphylococcus, one finds the same type of pus or purulent exudate in the joint space that one would find in a boil or carbuncle. This was not the case in the experimental streptococcal arthritis. The synovial fluid is easily aspirated, and we have done it repeatedly even as early as six hours after injection. We have found a considerable number of polymorphonuclear leukocytes in this aspirated fluid in the early stages. A rabbit's normal leukocyte count is about 10,000, or twice the normal for man. This might help to explain the larger number of polymorphonuclear leukocytes that are usually seen in this type of arthritis. It is well known that in rheumatoid arthritis the leukocyte count of the synovial fluid is often elevated to 25,000 and occasionally to 50,000 cells with a high percentage of polymorphonuclear leukocytes. We usually infer from this that the inflammatory process in the synovial fluid in cases of rheumatoid arthritis is often acute. If repeated injections of streptococci are given, one also produces a purulent arthritis. In reference to the question as to whether arthritis appeared in other joints after a longer time, I may say that we rarely observed joint involvement more than two weeks after injection. However, in a group of animals in which we have lowered the resistance by various means we have observed the development of arthritis in additional joints after an interval of thirty days subsequent to injection. I trust that we have not given the impression that we feel certain that there is an atypical pathologic picture for rheumatoid arthritis. We merely included this slide in order to demonstrate the type of disease process that we have attempted to reproduce.

#### The Treatment of Gonorrheal and Rheumatoid Arthritis with Sulfanilamide

DRS. HOWARD C. COGGESHALL and WALTER BAUER, Boston: In order to determine the value of sulfanilamide as a chemotherapeutic agent in the treatment of gonorrheal and rheumatoid arthritis, the following studies were undertaken:

1. Fourteen cases of proved and four cases of probable gonorrheal arthritis, two cases of uncomplicated gonorrhea, two cases of proved and two cases of probable gonorrheal prostatitis were carefully observed during and following the administration of large doses of sulfanilamide for periods of two weeks or longer.

2. The same large doses of sulfanilamide were administered for similar periods of time to ten patients suffering from mild to moderately severe rheumatoid arthritis of varying duration.

The dosage was calculated in the following manner: Three-fourths grain (0.15 Gm.) per pound (450 Gm.) of body weight was administered every twenty-four hours. In a few instances the initial dose equaled one-half the calculated twenty-four hour amount. This amount was readministered in four hours. Every four hours thereafter, the patient received one tenth of the calculated twenty-four hour amount. This method of administration results in sulfanilamide blood levels of 15 + mg. per hundred cubic centimeters. In most cases the initial dose and the dose administered every four hours, day and night, during the period of therapy equaled one sixth of the calculated twenty-four hour dose. This method of administration results in sulfanilamide blood levels of from 7 to 10 mg. per hundred cubic centimeters. Sulfanilamide when administered to persons with normal renal function is readily excreted. Therefore, if the necessary constant sulfanilamide blood levels are to be maintained throughout each twenty-four hour period, the drug must be administered every four hours day and night.

From the results obtained it would seem justifiable to conclude that sulfanilamide when administered in large doses for

two weeks or longer is a specific chemotherapeutic agent for certain strains of gonococci because: 1. Infected synovial fluids become sterile in from twenty-four to seventy-two hours after the institution of therapy. 2. In sixteen of the eighteen cases in which there was a proved genito-urinary focus, no gonococci were found after the third day of treatment. In one instance the genito-urinary focus did not become negative until the sulfanilamide blood level had reached 10 + mg. per hundred cubic centimeters. These seventeen patients remained clinically cured during the follow-up period. 3. The gonococcus complement fixation test failed to become positive in three cases of gonorrheal arthritis with infected synovial fluids. In nine of the remaining eighteen cases the complement fixation test became negative. 4. Nine of the proved and two of the probable cases of gonorrheal arthritis showed striking clinical improvement in from forty-eight to seventy-two hours after the institution of sulfanilamide therapy. The final end results in fourteen of the proved and four of the probable cases of gonorrheal arthritis were more satisfactory and took place in a shorter time than occurs with other forms of therapy. 5. The cases of gonorrheal arthritis in which an immediate clinical response occurred within forty-eight to seventy-two hours after the administration of sulfanilamide likewise showed a rapid fall in the erythrocyte sedimentation rate to normal.

Our results to date indicate that the dose of sulfanilamide necessary to cure gonococcal infections varies greatly. In some instances clinical cures are effected when the free sulfanilamide blood level is maintained at 5 mg. per hundred cubic centimeters while other cases require levels of 10 mg. or higher. The largest percentage of clinical cures will be obtained in patients with gonococcal infections if sulfanilamide is administered in large doses. If improvement does not occur within seventy-two hours, it probably means that the dosage employed is not adequate and therefore should be increased. Early administration of the drug in adequate amounts can prevent joint destruction.

The clinical course of rheumatoid arthritis was not affected in the ten patients treated with large doses of sulfanilamide, thus suggesting that the agent responsible for rheumatoid arthritis is not susceptible to this type of therapy. The rapid erythrocyte sedimentation rates observed in this group remained unchanged.

The toxic manifestations resulting from sulfanilamide therapy are readily recognized. The majority of them do not represent serious complications. Cyanosis is always present in patients receiving large doses. The dyspnea and the reduction of the plasma carbon dioxide content is directly related to alterations in the electrolyte metabolism (unpublished data). We have not encountered acute hemolytic anemia during the administration of sulfanilamide but have observed a slow, progressive subclinical hemolytic anemia in twelve cases. Leukopenia was observed in two cases.

#### DISCUSSION

DR. T. DUCKETT JONES, Boston: The excellent results of Drs. Bauer and Coggeshall in treating gonorrheal arthritis are in no sense approached in rheumatic fever. We cannot even conclude that the clinical course is unaltered, as they do with regard to sulfanilamide in the treatment of rheumatoid arthritis. I had high hopes when the drug was first introduced that it might be effective either in the prevention or in the treatment of rheumatic fever. No encouragement has been reported to date for either. Swift has reported its ineffectiveness in eight cases and was led to conclude that the toxic action of the drug in active rheumatic fever far outweighs the beneficial therapeutic effect. In fact, from his protocols it is difficult to see that any ameliorating influence was noted. I have noted no definite beneficial effect on the course of rheumatic fever although I have tried it in fifty-eight cases in which varying degrees of severity of the disease occurred. Striking is the fact that thirty-one of the fifty-eight patients presented definite evidence of toxicity to the drug. The more severe the rheumatic fever, the more frequent and severe the reaction. It is dangerous in the seriously ill rheumatic fever subject, and I should strongly urge against its administration. I have encountered pulmonary edema in such patients. Because of

the frequency of the association of hemolytic streptococcus infection in conjunction with the onset and recurrence of rheumatic fever, it was at first thought that studies of etiologic significance might be obtained; but this hope was dispelled by Swift. He demonstrated, and I have confirmed the observation, that hemolytic streptococcus immune responses, as indicated by a rise in the antistreptolysin titer, occur in rheumatic fever subjects despite the use of sulfanilamide. A small group of rheumatic fever subjects having hemolytic streptococcus throat infections were treated with sulfanilamide in an attempt to prevent the development of recurrent rheumatic fever. Alternate patients were given salicylates as a control group. In each group (six each) there were two severe recurrences and a fatal issue in each. The only difference between the two groups was the evident comfort of the group treated with acetylsalicylic acid as compared to the patients receiving sulfanilamide. This does not completely settle the question of prevention of recurrences of rheumatic fever and I am sure that some one will ultimately present a study large enough to be of statistical value, in which the blood level of free sulfanilamide in rheumatic fever subjects is kept at a reasonably high level during the winter and spring seasons when hemolytic streptococcus infection and recurrent rheumatic fever are common. I should like to stress with the authors that large doses be given and spaced throughout the day, that the blood level of free sulfanilamide be frequently determined and kept at least near the 10 mg. mark, and that complete blood studies be made at frequent intervals. Only when these features are observed will it be possible to compare reports on the therapeutic value of sulfanilamide.

DR. M. HENRY DAWSON, New York: Since March 1937 I have treated thirty-two patients suffering from gonorrheal arthritis with sulfanilamide. The results, while favorable, have not been as brilliantly successful as those reported by Drs. Coggeshall and Bauer, but I think from their report that some of the reasons are apparent. In the first place, I have treated a large number of chronic and subacute cases and in some of these the results have been equivocal. In many of the acute cases I have had the same spectacular success which has been reported. In the second place, my patients for the most part have been treated in an ambulatory clinic where it has not been possible to give as large doses of the drug; indeed, the whole problem of dosage could not be controlled. There are now a large number of favorable reports in the literature concerning the value of sulfanilamide in gonococcal infections and the carefully controlled work reported by Drs. Coggeshall and Bauer is particularly conclusive. I should like to add a few words concerning a procedure which I have recently tried on resistant and subacute and chronic cases; that is, a combination of sulfanilamide and fever therapy. The procedure has been to employ more moderate degrees of fever than those customarily employed in treating this disease, usually from 104 to 105 F. for five or six hours together with sulfanilamide (1.2 Gm. every six hours). The results of this combined treatment have been almost uniformly successful and several cases which did not respond to the drug alone were quickly cured. Similar results have been reported by Ballinger, Elder and McDonald and by Cheetham and Roemer. The results obtained by Drs. Coggeshall and Bauer with the use of sulfanilamide alone have been so good that it may not be necessary to use combined therapy. In any case it would appear that we now possess highly effective methods for the treatment of this condition.

DR. PHILIP S. HENCH, Rochester, Minn.: In the past eight years great advances have been made in the treatment of gonorrheal arthritis. Although I certainly do not begrudge the victims of the disease their good fortune in now having at hand such successful measures for treatment, it has always seemed to me rather "unfair" that that much larger army, the poor victims of atrophic arthritis, must still wait for an equally rapid and successful treatment. At the moment some physicians are arguing the respective merits of fever therapy and sulfanilamide for gonorrhea and gonorrheal arthritis. But the argument will not long continue because any patient would rather take pills, even though they produce certain disagreeable symptoms, than endure the stress of prolonged sessions of fever therapy. Furthermore, current experiences indicate that, in general,

sulfanilamide is as promptly successful as is fever therapy. However, a small percentage of patients with gonorrhea and gonorrheal arthritis do not respond to the administration of sulfanilamide or cannot take it in effective amounts because of its toxicity for them. In my experience about 10 per cent of patients with gonorrhea either cannot tolerate sulfanilamide at all or cannot tolerate enough of it to be effective. When a patient with gonorrheal arthritis does not respond promptly after taking sulfanilamide for three or four days, we at the Mayo Clinic discontinue the drug at once and prescribe fever therapy without further delay in order to avoid the risk of serious articular destruction. Sometimes fever therapy is then promptly successful. There are certain particularly potent strains of gonococci that are resistant not only to sulfanilamide but also to fever. Against such strains the use of sulfanilamide combined with fever therapy is at times effective; sometimes it is not. At the Mayo Clinic we have been using, in general, about two-thirds the amount of sulfanilamide advocated by Drs. Coggeshall and Bauer; perhaps our doses were inadequate in some cases. However, Dr. Cook of our urologic department has generally found that patients who did not respond to a daily dose of from 60 to 80 grains (4 to 5.3 Gm.) of sulfanilamide usually failed to respond also when the dose was increased to 100 or 120 grains (6.5 to 8 Gm.) daily. We have been disappointed with the results of sulfanilamide in the treatment of atrophic arthritis and rheumatic fever. In such conditions the patients have not been significantly benefited and marked toxicity frequently has developed. In almost the first case of atrophic arthritis in which we used this treatment a serious agranulocytosis developed but the patient fortunately recovered; this was the first instance of this kind brought to the attention of the American dispensers of the drug. In another case of atrophic arthritis, chills and fever (to 105 F.) occurred for four days; these symptoms subsided promptly when the administration of sulfanilamide was stopped. In still another case of atrophic arthritis fever (102 F.) occurred daily, associated with prostration and anorexia; although the administration of the drug was promptly stopped, these symptoms persisted for about three weeks. Although these poor results from sulfanilamide do not entirely contradict the hemolytic streptococcus theories of atrophic arthritis and of rheumatic fever, they do put the adherents of these theories on the defensive and I should like to hear some discussion on this point.

#### Neuropathic Joint Disease

DRS. KEENE O. HALDEMAN and RALPH SOTO-HALL, San Francisco: Certain diseases and injuries involving the spinal cord destroy the sensory protective mechanism of joints. Such joints, with single or repeated traumas, develop effusion and ligamentous relaxation, which is followed by the erosion of their cartilage, an irregular sclerosis of the subchondral bone, the production of parosteal bone, and intra-articular fractures which lead to a more or less complete disintegration of the joint. The absence of pain and the clinical and laboratory evidence of tabes dorsalis, syringomyelia or other cord lesions complete the picture of a neuroarthropathy, or so-called Charcot joint.

A series of forty-six patients showing neuropathic joint involvements in tabes dorsalis, syringomyelia, leprosy and traumatic paraplegia have been studied. The records of the forty patients suffering from tabetic arthropathies were tabulated according to the age, sex and joint involvement and certain clinical and laboratory observations. The proportion of males to females with such arthropathies is similar to the sex incidence of tabes dorsalis. The great majority of joint involvements appear between the ages of 40 and 60 years, at an average of twenty years after the occurrence of the primary lesion of syphilis.

Charcot joints most frequently occur in the lower extremity, the knee joint being the usual site of involvement. The positive clinical evidence of rigid pupils and absent knee jerks is of much greater importance than the various tests performed on the blood and spinal fluid in the diagnosis of a tabetic arthropathy. In an early stage of the neuropathic joint disease, its progress may be halted by the use of a protective brace.

We have adopted a method of producing the fusion of a Charcot joint in two stages. A preliminary drilling of the ends of the bones making up the joint is done for the purpose of

increasing their osteogenic power, followed in six weeks by the usual arthrodesing operation. Such a procedure in five cases resulted in firm bony fusion in three instances, with the final result not yet determined in the remaining two.

#### DISCUSSION

DR. L. MAXWELL LOCKIE, Buffalo: It is surprising that so many of these patients show a multiplicity of the joint involvement of the Charcot type. Many physicians erroneously dismiss the diagnosis of syphilitic joint disease if the blood Wassermann reaction is negative.

DR. ROBERT WARTENBERG, San Francisco: This study reminds us that there is such a definite clinical entity as the tabetic neuropathic joint, and that it is not, as Virchow believed, simply a modified arthritis deformans occurring in a tabetic patient. There are three theories of pathogenesis. The first considers the tabetic joint as due to an avascular, inflammatory process, from a syphilitic arteritis, phlebitis and osteitis. This theory can be easily disproved. The clinical picture of the two diseases is quite different. The "mechanical" theory states that the tabetic joints are essentially traumatic in origin and due to a combination of analgesia, hypotonia, loose joints, osteoporosis and ataxia. The tabetic patient maltreats his joints and doesn't feel it. Generally speaking, it is inconceivable that the normal use of the limbs and the spine could produce, even if the sensibility is lost, such grotesque bone proliferation and bone destruction as are found in tabetic joints. There is no adequate relationship between cause and effect. It is a clinical fact that tabetic joints may be demonstrable, especially by x-ray examination, at an early period of the tabes when there is no ataxia and no analgesia. They may develop in bedridden patients and appear often acutely. Sometimes the analgesia is not complete and yet the joint changes are profound. This theory cannot explain the "mal perforans" which often accompanies the tabetic joint or the arthropathies in syringomyelia where there is no ataxia. To support the mechanical theory, experimental work on cats has been done: the posterior roots have been cut, the limbs rendered anesthetic and traumatized. Arthropathies similar to those of the tabetic were claimed to be thus produced. But in addition to the sensory fibers which were cut in these experiments, they have in all probability also to do with transmission of trophic impulses. The third, the trophic, theory considers as the fundamental pathogenic factor in the production of tabetic joints the disturbance in the nervous trophic regulation. Although the trophic state of the tissues is essentially the function of the tissue cells themselves and there are in all probability no specific trophic fibers, a trophic regulatory influence of the nervous system must be assumed. The trophic impulses avail themselves of other tracts, such as motor, vasomotor, secretory and sensory fibers which are capable of antidromic conduction. Certain manifestations in tabes point to their possible sympathetic origin: subcutaneous and intestinal hemorrhages, visceral pain attacks, secretory crises, i. e. gastrorrhea, sialorrhea, galactorrhea. Interesting in this regard are the recently discovered local disturbances in sympathetic vessel innervation found in unilateral tabetic arthropathies, especially in the neighborhood of the affected joints. The following pathologic disturbances were found: elevation of the local temperature, rise in the arterial and venous blood pressure, increase of the oscillometric index, anomalies of the sweat secretion and disturbances in the pilomotor reflex. These clinical observations, together with the postmortem changes, indicate the role of the sympathetic nervous system in this disease and possibly also in the production of tabetic joints. The trophic influence is exerted by a reflex arc in the same way as is the motor influence. The centripetal limb of this arc probably goes through the sensory fibers, the centrifugal through the vasomotor fibers. The lesion which produces trophic disturbances may lie at any point of these two limbs or at their juncture. It is essential for the understanding of pathologic trophic changes to bear in mind that the trophic state of the tissues is much more influenced by a pathologic change of this nervous regulation than by a complete cessation. The cardinal sign of tabes, ataxia, is due to the fact that the outgoing motor impulses are not properly regulated by the incoming sensory impulses. In tabes the nervous trophic regulation is disturbed in the same way as the motor mechanism. In both instances the reflex arc is disturbed, and in both instances there is too much or too little innervation.

In the tabetic joints, both grotesque bone proliferation and bone destruction occur. By this trophic-ataxia theory the pronounced influence of ataxia and trauma can be easily explained. Asher, has demonstrated that a skin with disturbed sympathetic innervation shows diminished resistance. In the same way the trophic regulation of tabetic joints thus far maintained fails when ataxia, loose joints and so on put too severe requirements on the joints. The whole problem is still not solved and the words of Virchow in 1854 "The trophic influence of the nerves is still a dark chapter" even now hold true.

DR. J. ALBERT KEY, St. Louis: What happens in Charcot joints is not due to trauma and is not due to a change in the blood vessels. There is a decrease in the toughness of the tissue; this change is not limited to the bone and cartilage. The ligaments disintegrate. This is not due to the loss of muscle tone. Persons who walk year after year with infantile paralysis develop deformities; the weak muscles stretch and their ligaments are put to tremendous abnormal strains. Their articular surfaces are subjected to mechanical insults far greater than occur in Charcot joints, yet the articular surfaces remain in good condition. So I am perfectly sure in my own mind that in Charcot joints there is a trophic change and that that change affects the white fibrous tissue—not only the white fibrous tissues of the ligaments but the cartilage and the bone. The bone loses its toughness and disintegrates, and so does the cartilage. It is obvious that tabetic patients don't have any difficulty in producing bone. I have always thought that the reason Charcot joints were considered difficult to operate on and fuse was that the patients are difficult to treat. The muscles have lost their tone, there is nothing to hold these bone ends together, and mechanical fixation is necessary. Some years ago I published a paper in which I advised putting a pin through the tibia, another through the femur and pulling them together with turnbuckles and that worked all right. Bone is more apt to unite if one bores holes in it in an attempt to convert the hard compact bone to a soft, spongy cancellous bone, because new channels for bone to grow are opened. I think this method of Drs. Haldeman and Soto-Hall of doing it in two stages is a good one.

DR. H. H. MANN, Los Angeles: How would you diagnose a case of tabes in which the symptoms are in the hip joint, and the x-ray examination shows a reduction in joint space? As rheumatoid arthritis, tuberculosis, or Charcot joint? Would the sedimentation rate be of any value?

DR. C. L. STEINBERG, Rochester, N. Y.: For several years I have observed a neuropathic syndrome associated with atrophic or rheumatoid arthritis. This syndrome is characterized by catarrhal involvement of the cochlear division of the acoustic nerve. The vestibular root escapes injury. The "nerve" deafness is associated with exacerbations of the arthritis. These people become quite deaf during exacerbations and have normal or almost normal hearing with remissions or "cure" of the arthritis. This syndrome has been observed not infrequently in the third and fourth decades. The improved hearing noted in this group might be due to the remission or it might occur from the large doses of vitamin B<sub>1</sub> that I have been employing in their treatment. For the past two years I have been giving my arthritic patients a minimum of 400 B<sub>1</sub> units daily for its possible analgesic action. The analgesia has not occurred but auditory improvement has been noted. Drummond in 1934, Selfridge in 1937 and several other otologists have described some types of eighth nerve deafness that responded to vitamin B<sub>1</sub>. Selfridge has apparently been able to produce a progressive degeneration of the eighth nerve in animals fed a deficient vitamin B<sub>1</sub> diet. May not the increased demand for vitamin B previously suggested in a recently published article account for the eighth nerve involvement in arthritis?

DR. KEENE O. HALDEMAN, San Francisco: We believe that the differential diagnosis in involvement of the hip rests primarily on the absence of pain and on the proliferative changes which one occasionally sees. Most of our cases of Charcot hip had a fracture and then went on to a disintegration of the hip. In our entire series of forty tabetic arthropathies, eighteen patients gave a history of fractures, which often seemed to initiate the changes in the involved joint.

(To be continued)

## Current Medical Literature

### AMERICAN

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Titles marked with an asterisk (\*) are abstracted below.

### American Journal of Pathology, Boston

14: 515-690 (Sept.) 1938

Malignant Giant Cell Tumor of Bone. F. W. Stewart, B. L. Coley and J. H. Farrow, New York.—p. 515.

Blood Plasma Proteins as Influenced by Liver Injury Induced by Carbon Tetrachloride and Gum Acacia. C. C. Erickson, G. P. Heckel and R. E. Knutti, Rochester, N. Y.—p. 537.

Comparative Morphologic Study of Mammary Gland in a High and a Low Tumor Strain of Mice. Elizabeth Fekete, Bar Harbor, Maine.—p. 557.

\*Studies on Infectious Agent of Inclusion Blennorrhoea. L. A. Julianelle, R. W. Harrison and A. C. Lange, St. Louis.—p. 579.

\*Phagocytic Activity of Human Leukocytes, with Special Reference to Their Type and Maturity. A. J. Hertzog, Minneapolis.—p. 595.

Lymph Node Metastasis of Sarcoma. S. Warren and R. W. Meyer, Boston.—p. 605.

Primary Liposarcoma of Bone: Report of Case. J. Duffy and F. W. Stewart, New York.—p. 621.

**Infectious Agent of Inclusion Blennorrhoea.**—In trying to prove that inclusion blennorrhoea and trachoma are separate entities, Julianelle and his associates studied the twenty-two cases of inclusion blennorrhoea admitted to the ophthalmologic clinic of Washington University, the St. Louis Maternity Hospital (three) and the Bethesda Hospital of St. Louis (one). Diagnosis was verified by a search for the characteristic inclusions. Material for study consisted of a suspension of tissue fragments obtained by scraping (for therapeutic purposes) the conjunctiva of the everted lid. The tissues thus removed were emulsified in 1 cc. of veal infusion broth ( $p_H$  7.6 to 7.8). The suspension of tissues was always triturated under sterile conditions, without the intervention of abrasive substances, immediately on return to the laboratory. In testing the infectivity of the tissues, inoculations were made by direct swabbing from patient to animal (apes and monkeys), by swabbing with the suspension of tissues or by injection. A corollary experiment was conducted in which animals recovering from experimental inclusion blennorrhoea were inoculated at a later date with active material from trachoma. It was not possible to show that the former infection offered any protection to the later inoculation. The studies suggest that the infectious agent of inclusion blennorrhoea is not bacterial. It appears to be a virus capable of inducing specific infection in monkeys after passage through Berkefeld V and collodion filters, in this respect corroborating and amplifying experiments of other observers. Analysis of the individual manifestations reveals that both in spontaneous and in experimental infection there is a shortening of the incubation period and duration in inclusion blennorrhoea. While in appearance the two diseases are similar in the monkey, in man trachoma only induces cicatrization, corneal complications and impairment of visual acuity and exhibits a marked tendency toward recurrence after apparent healing. Silver nitrate has been found to be an effective therapeutic agent in trachoma but not in inclusion blennorrhoea. Trachoma, moreover, occurs only in the eye and its adnexa, while inclusion blennorrhoea is essentially a genital infection transmitted from the mother to the infant before birth. While there can be no doubt that the two ocular infections are clinically different, any and all of the differential characteristics may be due as much to variations in degree of pathogenicity of the strains of virus involved as to any actual distinctions in species. The inability of both viruses to survive serial animal passage, stimulate immunity and initiate artificial propagation and the resemblance of the respective inclusions suggest that the two viruses fall within the same or

closely related biologic groups. Other authors have considered the infectious agent of inclusion blennorrhoea to be the inclusion body itself. The present study offers no information to support or refute this opinion.

**Phagocytic Activity of Human Leukocytes.**—Hertzog studied the phagocytic activity of the leukocytes from seventeen cases of leukemia, three cases of infectious mononucleosis, four cases of lymphocytosis and two cases of eosinophilia. Staphylococci and streptococci were used as test particles. The mature polymorphonuclear neutrophils showed the greatest amount of phagocytosis both as to the number of bacteria ingested per cell and as to the percentage of cells engulfing bacteria. The monocytes, eosinophils and metamyelocytes were also actively phagocytic. The phagocytic activity of the myelocytes, promyelocytes, leukoblasts and myeloblasts appears to be directly proportional to the maturity of the cell, as there was a marked decrease in phagocytosis in the more immature forms. An exception was found in the histoid stem cell and histoid monoblast of leukemic reticulo-endotheliosis, as these immature cells showed an unusual degree of phagocytosis. Phagocytosis was observed in a small proportion of mature lymphocytes. The degree of phagocytosis increased as the cell grew larger with a corresponding increase in cytoplasm. The leukocytoid lymphocyte of infectious mononucleosis showed the greatest phagocytic activity. Hence, lymphocytes in their prephagocytic stage may occasionally show phagocytosis under experimental conditions.

### American Journal of Psychiatry, New York

95: 255-508 (Sept.) 1938

The Likeness of Cortical Dysrhythmias of Schizophrenia and Psychomotor Epilepsy. F. A. Gibbs, E. L. Gibbs and W. G. Lennox, Boston.—p. 255.

Treatment of Schizophrenia with Insulin Shock: Personal Experiences and General Review. A. H. Vander Veer, Chicago, and H. H. Reese, Madison, Wis.—p. 271.

Insulin Treatment of Psychoses: Suggested Mechanism. E. Ziskind and Esther Somerfeld-Ziskind, Los Angeles.—p. 291.

Metrazol Treatment in Schizophrenia: Study of Thirty-Five Cases in Private Practice, Complications and Their Prevention. N. W. Winkelman, Philadelphia.—p. 303.

Chart for Control and Recording of Insulin Shock Therapy. D. Goldman, Cincinnati.—p. 317.

Multiple Therapy in the Psychoses. H. H. Goldstein, E. F. Dombrowski and J. V. Edlin, Chicago.—p. 321.

Early Effects of Metrazol Therapy in Chronic Psychotic Overactivity. L. H. Cohen, Worcester, Mass.—p. 327.

Histopathology of Psychoses with Subacute Bacterial and Chronic Verrucose Rheumatic Endocarditis. W. L. Bruchsch, Indianapolis.—p. 335.

Present Status of Fever Therapy in Prevention and Treatment of Neurosyphilis. A. J. Rosanoff, Los Angeles.—p. 347.

Effect of Adrenalin and Mecholyl in States of Anxiety in Psychoneurotic Patients. E. Lindemann and J. E. Finesinger, Boston.—p. 353.

\*Effective Use of Phenobarbital and Benzadrine Sulfate (Amphetamine Sulfate) in Treatment of Epilepsy. B. Cohen, North Grafton, Mass., and A. Myerson, Boston.—p. 371.

Observations on Confabulation. H. W. Williams and C. Rupp, Howard, R. I.—p. 395.

Ulcerative Colitis and the Personality. W. T. Brown, P. W. Preu and A. J. Sullivan, New Haven, Conn.—p. 407.

### Phenobarbital and Amphetamine Sulfate in Epilepsy.

—Cohen and Myerson found that phenobarbital adjusted individually with reference to the rhythm of each patient's seizures reduced the seizures in male patients by 69 per cent; of the ninety-three patients treated eighty-three were improved. Sixty-seven patients showed a 50 per cent reduction of seizures or better. Of fifty female patients forty-five were improved with a total seizure reduction of 61 per cent. Thirty-four patients showed 50 per cent reduction of seizures or better. Amphetamine sulfate (benzadrine sulfate) proved specific in the treatment of ataxia and drowsiness which developed in fifteen patients in the course of phenobarbital medication. The daily dosage of amphetamine varied from 5 to 20 mg. Amphetamine permits the retention of effective doses of phenobarbital otherwise impossible. It does not increase the number or the severity of the epileptic seizures. It has no apparent effect on the blood sugar, nonprotein nitrogen or creatinine or on the basal metabolic rate, pulse rate or blood pressure. There appears to be no necessity for routine catharsis in the treatment of epilepsy when phenobarbital dosage is adequate.



## American Journal of Surgery, New York

42: 1-286 (Oct.) 1938. Partial Index

- The Use of Orbicularis Palpebrarum Muscle in Surgery of the Eyelids. J. M. Wheeler, New York.—p. 7.
- Surgery of Secondary Glaucoma. A. Greenwood, Boston.—p. 10.
- Technic of Extraction of Intra-Ocular Foreign Bodies. W. B. Lancaster, Boston.—p. 14.
- \*Certain Postoperative Complications of Cataract Operations, with Especial Reference to Study of 1,004 Operations. C. Berens and D. W. Bogart, New York.—p. 39.
- Management of Complications of Intra-Ocular Surgery. E. L. Goar, Houston, Texas.—p. 62.
- Review of Some Modern Methods for Ophthalmic Plastic Surgery. E. B. Spaeth, Philadelphia.—p. 89.
- Aural Surgery: Theoretical and Technical Advances in Recent Decades. P. D. Kerrison, New York.—p. 103.
- Acute Encephalitis or Toxic Encephalopathy Simulating Brain Abscess. P. J. Zentay, St. Louis.—p. 112.
- Diagnosis and Treatment of Orogenic Meningitis. S. J. Kopetzky, New York.—p. 131.
- The Education of the Deaf and Hard-of-Hearing Child. M. A. Goldstein, St. Louis.—p. 151.
- Malignant Diseases of Paranasal Sinuses. G. B. New, Rochester, Minn.—p. 170.
- \*Dietary Treatment of Chronic Sinusitis. B. R. Shurly, Detroit.—p. 174.
- Deep Abscess of the Neck: Surgical Treatment. J. F. Barnhill, Miami Beach, Fla.—p. 207.
- Types of Laryngeal Obstruction and Their Treatment. L. Richards, Boston.—p. 239.
- Surgical Indications in Perforation of the Esophagus for Foreign Bodies. J. R. Head, Chicago.—p. 266.
- Benign Tumors and Tumor-like Conditions in Tracheobronchial Tree. C. Jackson and C. L. Jackson, Philadelphia.—p. 275.

## Postoperative Complications of Cataract Operations.

—Because many complications may be prevented Berens and Bogart analyzed the records of the 1,004 cataract extractions performed at the New York Eye and Ear Infirmary during the last two years. Extracapsular extractions were performed on 702 patients and intracapsular extractions on 302. The most frequent postoperative complications were hemorrhage into the anterior chamber (4 per cent in the intracapsular cases and 1.4 per cent in the extracapsular cases) and loss of vitreous (9.9 per cent in the intracapsular cases and 9 per cent in the extracapsular cases). The other complications, detachment of the retina, detachment of the choroid, suppurative intra-ocular infection and prolapse of the iris, occurred in only a few cases of each series. Secondary glaucoma occurred in seven extracapsular cases; iridocyclitis was observed following seven extracapsular extractions and two intracapsular operations. If the number of postoperative complications is to be reduced, there seems to be little question that the preliminary examination is most important. Careful preoperative study of the patients, combined with the institution of treatment for chronic infections, hyperglycemia, hypertension and other general diseases when found may prevent serious postoperative complications which frequently result in impaired vision or blindness. Careful complete suturing of the wound with a complete but not too wide conjunctival flap seems to be one of the best methods of preventing many serious postoperative complications. In the postoperative care of the patient the most important single factor in preventing complications (other than careful nursing, the treatment of cough as well as other movements which might endanger the eye) is the careful postoperative examination of the eye, especially the avoidance of squeezing by unnecessary or clumsy manipulation.

**Dietary Treatment of Chronic Sinusitis.**—In summary, Shurly points out that the treatment of chronic sinusitis calls for surgical intervention. Dietetic treatment should be used as a therapeutic aid. Prophylactic treatment in early infancy may offer much in preventing bony malformations of the nose and sinuses, through the proper use of vitamin D, particularly in milk, eggs and leafy vegetables. Vitamin A deficiency may influence the resistance to infection, with lowered vitality of tissues, especially in the ear, nose and throat. Vitamin C has a special influence on the mucous membranes of the gums, nose and mouth. The value of raw vegetable juice and mineral salts lies in promoting cell growth and selection. Special attention to endocrine balance with the use of iodine and thyroid extracts is of value in establishing vasomotor tones. Food allergy must be determined by special tests and the history. The prevention of sinus infection at the time of the removal of tonsils and adenoids may require special dietetic treatment and cod liver oil.

## Annals of Surgery, Philadelphia

108: 481-800 (Oct.) 1938

- Address of the President: Relation of Surgeon and Hospital. A. W. Elting, Albany, N. Y.—p. 481.
- Need of a National Council on Medical Education, Licensure and Hospitals. W. C. Rappleye, New York.—p. 489.
- Treatment of Cranial Osteomyelitis and Brain Abscess. A. W. Adson, Rochester, Minn.—p. 499.
- \*Rapid Control of Intracranial Pressure. E. R. Schmidt, Madison, Wis.—p. 520.
- Progressive Exophthalmos Associated with Disorders of Thyroid Gland. H. C. Naffziger, San Francisco.—p. 529.
- Injuries to Recurrent Laryngeal Nerve in Thyroid Operations: Their Management and Avoidance. F. H. Lahey and W. B. Hoover, Boston.—p. 545.
- \*Amount of Thyroid Tissue to Be Left in Operations for Diffuse Toxic Goiter. M. K. Smith, New York.—p. 563.
- Iodine Metabolism in Exophthalmic Goiter. G. M. Curtis and I. D. Puppel, Columbus, Ohio.—p. 574.
- Mediastinitis Following Cervical Suppuration. H. E. Pearce Jr., Rochester, N. Y.—p. 588.
- The Management of Certain Lesions of the Esophagus. G. C. Penberthy and C. D. Benson, Detroit.—p. 612.
- Lymphatic Spread of Carcinoma of Rectum. R. K. Gilchrist and V. C. David, Chicago.—p. 621.
- \*Arteriovenous Aneurysms. M. R. Reid and J. McGuire, Cincinnati.—p. 643.
- Spontaneous Arteriovenous Fistula Between Abdominal Aorta and Inferior Vena Cava: Case Report. E. P. Lehman, University, Va.—p. 694.
- Congenital Arteriovenous Fistula or Fistulas: Case Report. W. D. Wise and E. T. Lisansky, Baltimore.—p. 701.
- Heminephrectomy in Disease of the Double Kidney: Report of Fourteen Cases. E. Beer and W. H. Mencher, New York.—p. 705.
- Denervation of Bladder for Relief of Intractable Pain. W. J. M. Scott and C. F. Schroeder, Rochester, N. Y.—p. 730.
- Repair of Abdominal Incisions. A. O. Whipple and R. H. E. Elliott Jr., New York.—p. 741.
- Spontaneous Rupture of Superior and Inferior Epigastric Arteries Within Rectus Abdominis Sheath. R. L. Payne, Norfolk, Va.—p. 757.
- The Replacement of Sodium Chloride in Surgical Patients. F. A. Collier, R. M. Bartlett, D. L. C. Bingham, W. G. Maddock and S. Pedersen, Ann Arbor, Mich.—p. 769.

**Rapid Control of Intracranial Pressure.**—The method for controlling intracranial pressure that Schmidt recommends depends on mechanics alone, is rapid, and he thinks effective in most cases. The method consists of inserting a No. 6 French ureteral catheter through a trephine opening in the skull. The ventricle is first punctured with an ordinary ventricular puncture needle in order to make a path. Into the ureteral catheter the stylet of the ventricular needle is placed, so as to make it firm. The stylet and catheter are introduced into the ventricle through the previously formed path made by the ventricular puncture. The catheter is anchored with a fine linen suture to the skin. The top of the catheter should be a little above the skin to prevent the skin from closing over the catheter. A 1:2,000 red mercuric iodide dressing is placed over the end of the catheter. If the catheter becomes occluded it is opened by inserting a long needle into it and aspirating. Suppuration may develop at the skin after a week or more and the catheter has to be removed and inserted on the other side. However, the catheter may be kept for longer periods, depending on the development of suppuration at the skin. The author has used this method in twenty-four cases and found it to be of aid in reducing increased intracranial pressure preoperatively and postoperatively, to stabilize patients who have had pressure for some time, to aid in diagnosis, to reduce emergency operations after ventriculograms or in acute or high intracranial pressure, and to heal the skin over a cerebral hernia. Owing to the danger of introducing infection, one must use the procedure carefully and only after weighing the indications.

**Thyroidectomy and Remaining Tissue.**—For a number of years Smith has measured remnants of thyroid equal to those remaining by cutting out portions of corresponding size from the specimens removed and weighing them, thus arriving at an estimate of the amount of tissue left in the neck. Seventy-five patients with diffuse toxic goiter in whom this procedure has been carried out and who have been followed with metabolism tests for from eight months to six years form the basis of his study. The fact that relapses occurred in 13 per cent of the cases, a figure that may well be increased after a longer period of observation, would argue that criticism might point rather toward too great conservatism than otherwise. The estimated size of the remnants of thyroid left in the neck has ranged between 3 and 25 Gm. Thirty-seven were recorded as 6 Gm.

or less and thirty-eight as 7 Gm. or more. The most important factors in planning the extent of operation is the severity of the disease and the size of the gland. When the incidence of persistent and recurrent cases is used as a criterion, the results favored the smaller remnants on the basis both of actual weight and of relative proportion. Examination of the individual failures showed that in no case did the remnant fall into the smaller half of the series on both counts. This indicates that one must be guided in his judgment by the size of the original goiter and in the case of small toxic glands be particularly radical. On the basis of his study the author thinks that a remnant of 4 or 5 Gm. as he has estimated it or, as corrected, 6 or 7 Gm. should result in fewer failures. Blocks of tissue measuring 3 by 1 by 1 cm. seem to be a satisfactory amount of tissue to allow to remain on each side of the trachea in the more toxic cases unless the gland is small. In the case of medium to good sized glands a remnant of 5 Gm. would represent a small proportion of the original goiter, say one tenth or less, a relative amount which in the series studied was followed by a low incidence of postoperative hyperthyroidism. In the case of glands which are little larger than normal, despite a marked toxicity, one should leave smaller amounts than usual so that the relative reduction of thyroid tissue is thorough. In large glands with only mild toxicity, more generous remnants ought to meet the indications.

**Arteriovenous Aneurysms.**—Reid and McGuire present another series of thirty cases of aneurysms (twenty-one arteriovenous aneurysms and nine cirroid), discuss the clinical observations and surgical procedures and supplement these clinical studies whenever pertinent by arteriovenous aneurysms produced experimentally in dogs. Sixteen of the arteriovenous aneurysms were operated on and all of them, except one of pulsating exophthalmos, were cured. In two instances the aneurysms healed spontaneously without operation. All of the nine cirroid aneurysms were operated on; three were cured and the other six were improved. There were no deaths in the entire series. There were eight arteriovenous aneurysms which had caused definite cardiac damage; in two there was severe cardiac decompensation. Of the nine cirroid aneurysms, two showed evidences of some cardiac damage. In every instance in which the heart was demonstrably affected, closure or excision of the fistula was followed by cardiac improvement. In the artery and vein opposite the fistula extensive calcification was noted in the walls of the vessels. In eleven, definite enlargement and thinning of the wall of the proximal artery was present. In many cases the wall of the involved vein was definitely hypertrophied. There was no positive evidence that the circulation time was definitely affected by the fistula. The authors' studies fail to confirm the observations of Holman and others who have reported a large increase in blood volume in cases of arteriovenous aneurysms. Slowing of the pulse rate when the fistula was closed was observed in ten cases and in the experimental animals. The extent of this slowing of pulse rate varied greatly and seemed to be directly related to the seriousness of the cardiac damage and the size of the fistulas. Venous pressures appear unaffected by arteriovenous aneurysms unless there is some evidence of cardiac decompensation, when the changes in venous pressures are similar to those which occur in cases of cardiac decompensation from any other cause. A rise in both systolic and diastolic pressures following closure of arteriovenous fistulas was observed in thirteen cases. That an extensive collateral circulation occurs around an arteriovenous fistula was confirmed in six instances. It is this overabundant collateral circulation which makes the occurrence of gangrene after excision of chronic arteriovenous fistulas practically unknown. The circulation, considerably distal to the fistula, may be impaired as evidenced by absent pulses, coldness of the part, cyanosis and occasional chronic ulcers that will not heal. Nerve paralyses associated with the arteriovenous condition occurred in four cases. Intracranial arteriovenous aneurysms developed in three cases, pulsating exophthalmos in two and a fistula between the ophthalmic vessels behind the eyeball in one. Two arteriovenous aneurysms healed spontaneously. A long period of rest in bed, with elevation of the affected part and the limitation of the intake of fluid, possibly bleeding, soon after the accident, might result in more spontaneous cures. Unless immediate or early operations are required because of

hemorrhage, dangerous hematoma, infection or rapid cardiac damage, it is wise to postpone the operation for from three to six months after the occurrence of the fistula. The essential thing in the operative treatment of arteriovenous and cirroid aneurysms is to eliminate all possibilities of any blood ever again passing through the fistulas. An easy method of making an arteriovenous fistula which can be alternately closed and opened is illustrated.

### Archives of Neurology and Psychiatry, Chicago

40: 639-856 (Oct.) 1938

- Studies on the Human Neuromuscular Mechanism: II. Effect of Ventromedial Chordotomy on Muscular Spasticity in Man. P. C. Bucy, Chicago.—p. 639.
- Studies in Diseases of Muscle: IV. Metabolism of Creatine and Creatinine in Muscular Wasting Subsequent to Disease of the Nervous System. A. T. Milhorat and H. G. Wolff, with technical assistance of V. Toscani, New York.—p. 663.
- Id.: V. Metabolism of Creatine and Creatinine in Myotonia Congenita, Myotonia Atrophica, Amyotonia Congenita, Dystonia Musculorum Deformans and Paralysis Agitans. A. T. Milhorat and H. G. Wolff, with technical assistance of V. Toscani, New York.—p. 680.
- Enuresis and Other Factors in Normal and in Psychotic Persons: Comparative Study of Incidence and Intercorrelations. J. J. Michaels, Boston, and Sylvia E. Goodman, Ann Arbor, Mich.—p. 699.
- Cerebral Impaludation. M. Ducoste, Villejuif, France.—p. 707.
- \*Eunuchoidism: Psychiatric and Endocrine Study of Six Cases. H. T. Carmichael and A. T. Kenyon, Chicago.—p. 717.
- Dependence of Sensation of Pain on Cutaneous Impulses. E. Hollander, New York.—p. 743.
- Pathogenesis of Syringomyelia: Case Illustrating the Process of Cavity Formation from Embryonic Cell Rests. K. Tamaki and A. J. Lubin, San Francisco.—p. 748.
- The Involuntary Melancholia Process. H. D. Palmer and S. H. Sherman, Philadelphia.—p. 762.
- Athetosis and Pallidal Deficiency. J. W. Papez, Ithaca, N. Y.; J. Hertzman, Cincinnati, and R. W. Rundles, Ithaca, N. Y.—p. 789.
- Etiologic Study of Landry's Original Case of Acute Ascending Paralysis. Madeline R. Brown, Boston.—p. 800.
- Herniation of the Brain Not Heretofore Described. I. Finkelman, Chicago.—p. 803.
- The Centenary of Multiple Sclerosis. T. J. Putnam, Boston.—p. 806.

**Eunuchoidism.**—Carmichael and Kenyon made a clinical study of six eunuchoids from the physical, endocrine and psychiatric points of view. In addition they estimated the urinary excretion of androgen and estrogen and administered extracts of the urine of pregnant women in attempts at therapy. In each instance the development of the secondary sex characters was that of the normal boy aged from 12 to 15. The basal metabolic rate was usually within the lower limits of normal. The patients were thin, fat or of ordinary build. The ratio of sitting to standing height varied from 47.2 to 52.8 per cent, and only one of the eunuchoids, who was very fat, approached closely the average normal value of 52.9. The ratio of span to stature varied from 105.5 to 110 per cent, being in all instances well in excess of the averages for most races cited by Hrdlička. The arms and legs were therefore disproportionately long. The six eunuchoid persons studied showed an average value of 20 international units of androgenic material in the urine daily with the fifteen minute hydrolysis (as compared with approximately 67 international units), with a range of from 7 to 33 units. Seven assays on four of these patients, studied by the two hour hydrolysis method, gave an average of 11 international units, with a range of from 0 to 17 units, as compared with the normal average of 40 units. Thus, no matter what duration of hydrolysis is chosen, the eunuchoid patients excreted about a third of the normal amount of androgenic material. Five eunuchoid patients studied for estrogenic material excreted the equivalents of 2, 2, 1, 2 and 7 micrograms of estrogen respectively, as compared with the normal of 10 micrograms. During treatment with large amounts of an extract of the urine of pregnant women for six months or more there was slight enlargement of the penis and increase in erections in two cases. In one case such treatment was accompanied by definite advances in sexual development at the age of 29, similar to the changes observed in normal boys at puberty; whether these changes were coincidental in this instance or were brought about by the treatment cannot be determined. Psychiatric study revealed nothing characteristic for the group. One patient could be classified as of dull normal intelligence, on the basis of an intelligence quotient of 83 in the Stanford-Binet test. In the remaining cases the intelligence ranged from this point to the intellectual capacity

required for successful college and professional work. The personalities of the patients varied from that of an active, energetic, popular, friendly, successful professional man to that of a quiet, withdrawn, sensitive shy, self-conscious person or of an overfastidious, perfectionistic, pious, ambitious, quiet, reserved man who suffered keenly from his physical inferiority to the point of feelings of reference, depression and suicidal thoughts and who tried to solve his problems finally by seeking refuge in training for the priesthood. The six patients sought treatment voluntarily. It is suggested that psychoanalysis of eunuchoid patients may prove an important contribution to an understanding of the relation of the endocrine glands to mental disorders.

### Endocrinology, Los Angeles

23: 393-534 (Oct.) 1938

- \*Endocrine Theories of Dysmenorrhea. C. F. Fluhmann, San Francisco.—p. 393.
- Hormone and Electrolyte Studies of Patients with Hyperadrenocortical Syndrome (Cushing's Syndrome). Evelyn Anderson, W. Haymaker and M. Joseph, Berkeley and San Francisco.—p. 398.
- Oral Therapy in Adrenal Insufficiency: Efficacy of Concentrated Adrenal Cortical Extract Preserved in Glycerol. G. W. Thorn, K. Emerson Jr. and H. Eisenberg, Baltimore.—p. 403.
- Effect of Thyroxine on Extent of Regeneration in Enucleated Adrenal Gland of the Rat. D. J. Ingle and G. M. Higgins, Rochester, Minn.—p. 419.
- Effect of Administration of Carbon Tetrachloride on Extent of Regeneration in Enucleated Adrenal Gland of the Rat. G. M. Higgins and D. J. Ingle, Rochester, Minn.—p. 424.
- Chick Thyroid Responses as a Basis for Thyrotropic Hormone Assay. G. K. Smelser, New York.—p. 429.
- Urinary Thyrotropic Hormone. K. Emerson Jr. and W. C. Cutting, Baltimore.—p. 439.
- Effect on Growth Rate of Thyroparathyroidectomy in Newborn Rats and of Subsequent Administration of Thyroid, Parathyroid and Anterior Hypophysis. Theodora Nussmann Salmon, New York.—p. 446.
- Effect of Long-Term Injections of Testosterone on Guinea Pig Endometrium. Doris Phelps, J. C. Burch and E. T. Ellison, Nashville, Tenn.—p. 458.
- Excretion and Fate of Androgens: II. Concerning Conversion of Androgens to Estrogens. C. D. Kochakian, Rochester, N. Y.—p. 463.
- The Physiologic Response of Ocular Transplants of Seminal Vesicle in Female Rabbits. R. H. Melchionna and Sarah Flanders, New York.—p. 468.
- \*Inhibition of Lactation During Puerperium by Testosterone Propionate. R. Kurzrok and C. P. O'Connell, New York.—p. 476.
- Inadequacies of Estradiol Substitution in Ovariectomized Albino Rats. H. Lauson, C. G. Heller and E. L. Sevringhaus, Madison, Wis.—p. 479.
- Skeletal Changes and Blood Serum Calcium Level in Pigeons Receiving Estrogens. C. A. Pfeiffer and W. U. Gardner, New Haven, Conn.—p. 485.
- Study of Estrogenic Content of Tissues in Pregnancy. F. Parker Jr. and B. Tenney Jr., Boston.—p. 492.
- Effect of Estrin on Gonad-Stimulating Complex of Anterior Pituitary of Parabolic Rats. E. Bunster and R. K. Meyer, Rochester, N. Y.—p. 496.
- Effect of Antuitrin-S on Thymus of Young Albino Rat. E. O. Butcher and E. C. Persike Jr., Clinton, N. Y.—p. 501.

**Endocrine Theories of Dysmenorrhea.**—In studying the problem of dysmenorrhea, Fluhmann determined the estrogenic content of the blood of nineteen women with severe dysmenorrhea. No pelvic or systemic cause for the painful menstruation was found. Eighty-five tests for estrogen were conducted by the mucification test; at least three on each patient were performed at weekly intervals. The blood estrogen of the nineteen patients failed to demonstrate any consistent departure from the normal, either in the amount of estrogen present or in the type of curves obtained. In eleven instances a single peak in the concentration of the substance occurred during the interval and presumably was associated with ovulation. In seven cases the interval rise was present, but a secondary increase also was noted at about the time of menstruation. The only abnormal observation was in a young woman of 19, in whom there was a definite increase of estrogen at the time of menstruation and no peak during the interval. There are serious objections to accepting any of the theories (deficiency of estrogen, excess of estrogen or deficiency of progesterin and overactivity of progesterin) which seek to explain the cause of primary dysmenorrhea solely as a hormone deficiency or excess.

**Inhibition of Lactation.**—Kurzrok and O'Connell injected twenty-one successive patients, in whom it was decided to terminate lactation, with testosterone propionate. The total dose ranged from 50 to 150 mg. Two doses were given daily for one or more days and all injections were made deep in the

gluteal region. The effect in only two instances was considered unsuccessful; one patient was completely relieved of symptoms on the fourth day and the other patient was injected with a total of 75 mg. of testosterone propionate divided into three doses. In the latter case the first injection was given on the first day post partum. The symptoms of pain, fullness and engorgement of the breasts were not relieved. In view of the fact that lactation usually begins on the fourth day post partum the inhibitory effect of testosterone propionate might have been exerted a little too early in this case. The results were excellent in the remaining nineteen cases. It was not unusual to find that, when doses of 25 mg. were given, complete relief of all symptoms was obtained within a few hours after the second dose (eight hours after the first dose). In general, 40 mg. or more of testosterone propionate was required to relieve all symptoms of engorgement of the breast. Complete relief of symptoms usually occurred within forty-eight hours. The best results were obtained from doses of 25 mg. each. Once the symptoms were relieved there was no tendency for their recurrence after the injections were stopped. There were no unpleasant by-effects from the treatment. The normal character of the lochia was not changed. No after-pains were produced. The onset of the first menstrual period was not delayed.

### Florida Medical Association Journal, Jacksonville

25: 157-212 (Oct.) 1938

- Quinine Amblyopia in Children. L. W. Holloway, Jacksonville.—p. 167.
- Abdominal Auscultation. J. H. Pound, Tallahassee.—p. 173.
- Malaria. M. M. Harrison, Bradenton.—p. 175.
- Peroral Endoscopy: Report of Cases. C. J. Heinberg, Pensacola.—p. 179.
- The Final Responsibility of Public Health Rests on the Medical Profession. A. B. McCreary, Jacksonville.—p. 181.

### Georgia Medical Association Journal, Atlanta

27: 377-418 (Oct.) 1938

- Urologic Conditions in Childhood. W. P. Jordan, Columbus.—p. 377.
- The Conservative Treatment of Chronic Pyelonephritis: A Brief Summary. S. T. Brown, Atlanta.—p. 380.
- Combined Sulfanilamide and Local Treatment of Gonococcal Infections. S. J. Sinkoe, Atlanta.—p. 382.
- The Management of Ureteral Calculi in Ambulatory Patients. M. F. Fowler and W. L. Champion, Atlanta.—p. 387.
- Hernia of the Urinary Bladder: Report of Cases. J. A. Hunnicutt Jr., Athens.—p. 393.
- Progress of Medicine in Georgia. G. A. T aylor, Augusta.—p. 398.
- House of Delegates of the A. M. A. Considers National Health Program. C. W. Roberts, Atlanta.—p. 405.

### Journal of Bone and Joint Surgery, Boston

20: 825-1126 (Oct.) 1938. Partial Index

- Treatment of Scoliosis by Wedging Jacket and Spine Fusion: Review of 265 Cases. A. D. Smith, F. L. Butte and A. B. Ferguson, New York.—p. 825.
- Correction of Extreme Flexion Contracture of Knee Joint. S. L. Haas, San Francisco.—p. 839.
- \*Sciatic Pain of Unknown Origin: Effective Method of Treatment. G. E. Haggart, Boston.—p. 851.
- Scalenus Anterior Muscle in Relation to Shoulder and Arm Pain. J. A. Freiberg, Cincinnati.—p. 860.
- Giant-Cell Tumor of Bone. B. L. Coley and N. L. Higginbotham, New York.—p. 870.
- Primary Hemangioma Involving Bones of Extremities. C. F. Geschickter and I. H. Maseritz, Baltimore.—p. 888.
- Bone Block for Painful Hips. J. B. L'Episcopo, Brooklyn.—p. 901.
- The Healing of Joint Fractures: Clinical and Experimental Study. K. O. Haldeman, San Francisco.—p. 912.
- Operative Technic for Hallux Valgus. M. A. Levine, Los Angeles.—p. 923.
- Recurrent Anterior Dislocation of Shoulder: Report of Eleven Cases Operated on by Method of Roberts. B. S. Burnet, Hot Springs National Park, Ark.—p. 926.
- Results of Treatment of Osteogenic Sarcoma. H. W. Meyerding, Rochester, Minn.—p. 933.
- Röntgenotherapy in Acute Osteoporosis: New Type of Treatment. E. B. Mumford, Indianapolis.—p. 949.
- Clinical and Anatomic Study of Semimembranosus Bursa in Relation to Popliteal Cyst. P. D. Wilson, A. L. Eyre-Brook and J. D. Francis, New York.—p. 963.
- \*Gas Bacillus Infection as Complication of Fractures. D. M. Bosworth, New York.—p. 985.
- Backache: Manipulative Treatment Without Anesthesia. F. A. Jostes, St. Louis.—p. 990.
- The Opera-Glass Hand in Chronic Arthritis: "La Main en Lorgnette" of Marie and Léri. L. S. Nelson, Brooklyn.—p. 1045.

**Sciatic Pain of Unknown Origin.**—Haggart outlines a method of treating sciatic pain that he has employed successfully in the treatment of seventy patients with sciatica of unknown origin. The method is also applicable for immediate

relief of severe sciatic pain while a clinical study is being made to determine the cause. The method is a combination of two, and in some instances of three, procedures: (1) perineural injection of the sciatic nerve with a 1 per cent solution of procaine hydrochloride with 2 drops of 1:1,000 epinephrine to the ounce, (2) traction to the affected extremity by the Russell method and (3) in an increasing number of cases manipulation of the lower part of the back under intravenous sodium ethyl (1 methyl-butyl) thiobarbiturate anesthesia. The objective of the injection, 50 cc., of the procaine hydrochloride is to surround the sciatic nerve with the solution and possibly also to inject its sheath. In addition, the fascia and substance of the piriformis muscle, and in some instances the posterior sacro-iliac ligament, are thoroughly infiltrated. Following injection and manipulation, with or without traction, all patients are instructed in muscular exercise of the lower part of the back and of the gluteal muscles. When the patients become ambulatory, posture training also is given as indicated. Intensive heat and massage are likewise utilized, chiefly applied to the lower part of the back, the region of the buttocks and the upper part of the thigh. Hot fomentations and infra-red rays have been the most effective forms of heat. Of the seventy-five patients, all but ten obtained immediate relief of pain. Thirteen were benefited temporarily for from three to six months. Ten patients were free of symptoms for one year and then did not return or answer follow-up letters. In thirty-eight cases it was eventually possible to make a definite diagnosis and so determine the cause of the sciatica and advise appropriate treatment.

**Gas Bacillus Infection as Complication of Fractures.**—Bosworth states that prophylaxis with both gas bacillus and tetanus antiserum should be the rule in all cases of compound fracture. Amputation should never be done for acute gas bacillus infection, although it may be necessary later because of deformity. Repeated massive doses of intravenous polyvalent serum should be continued until the infection is controlled. Drainage but not débridement should be instituted. Many tissues first thought to be dead will later be found viable. Roentgen therapy may yet prove to be of the greatest help. Orr dressings and treatment may be safely carried out as in any other infection of the bone, once the acute gas bacillus infection has been brought under control, without regard to the presence of *Bacillus welchii* and its associates which remain lying apparently inert in the wound.

### Journal of Lab. and Clinical Medicine, St. Louis

24: 1-110 (Oct.) 1938

- Differential Serum Vanadate Sedimentation Reaction. H. B. Hunt and D. L. Woodhouse, Birmingham, England.—p. 1.  
Trichostrongylus Colpophoriformis in the Human Appendix: Report of Case in Louisiana. J. R. Schenken and E. S. Moss, New Orleans.—p. 15.  
\*Massive Doses of Vitamin D in Chronic Arthritis: Its Effect on Calcium Metabolism. C. L. Steinberg, Rochester, N. Y.—p. 17.  
Studies on Anemia of Pregnancy in Gastroctomized and Normal Dogs. R. A. Bussabarger, F. P. Cuthbert and A. C. Ivy, Chicago.—p. 24.  
Tularemia Following Injury While Performing Postmortem Examination on Human Case: Report of Postmortem Findings in Case of Pulmonary Type of Tularemia. J. O. Weilbaecher Jr. and E. S. Moss, New Orleans.—p. 34.  
Difference in Growth of Pathogenic Fungi with Variation of Medium and Oxygen Tension. J. W. Williams, Cambridge, Mass.—p. 39.  
Physiologic Response of Pleural Surfaces to Implanted Dusts. W. R. Bradley and M. W. First, Detroit.—p. 44.  
\*Seasonal and Regional Factors in Acute Rheumatic Fever and Rheumatic Heart Disease. C. A. Mills, Cincinnati.—p. 53.  
Essential Hypertension of More Than Twenty-Five Years' Duration Showing No Renal Arteriolar Changes at Autopsy: Report of Case. S. Shapiro, New York.—p. 60.  
Effect of Liver Extract on Polycythemia Vera. R. H. Major, Kansas City, Kan.—p. 65.  
Reduction of Protosil Soluble by Urine. J. V. Scudi, New York.—p. 68.  
Culture versus Guinea Pig Inoculation in Diagnosis of Tuberculosis. W. A. Murphy and Dorothy Rhoades Duerschner, New York.—p. 70.  
Test for Occult Blood. E. Redowitz, Philadelphia.—p. 95.  
Methemoglobin Determination: Clinical Method. W. B. Wendel, Memphis, Tenn.—p. 96.

**Vitamin D in Chronic Arthritis.**—Steinberg studied the clinical effects of massive doses of vitamin D in the treatment of chronic arthritis and its possible effect on the blood calcium. He administered the vitamin in doses of 160,000 U. S. P. units daily to forty patients with chronic arthritis. Fourteen showed clinical improvement and twenty-six showed no improvement;

the condition of three of the latter group was definitely aggravated. The serum calcium and phosphorus levels of thirty-two patients were determined and it was found that massive doses of vitamin D will lower a high serum calcium; it will raise a low or normal serum calcium to a higher level and then, after continued administration, will again decrease the hypercalcemia level. The clinical improvement or nonimprovement or even aggravation of existing joint symptoms had no bearing on the change of blood calcium. The effect on the serum phosphorus was less marked. The effect of massive doses of vitamin D in chronic arthritis is nonspecific and the occasional improvement following its use is similar to that of the many other remedies employed in its nonspecific treatment. Even though the author feels that no specific virtues exist in such medication, at the same time he believes that its toxicity has been overemphasized, but he does not mean to imply that larger doses than he employed may not be dangerous or even fatal.

**Climatic Factors in Acute Rheumatic Fever.**—Mills presents evidence which indicates that some factor concerned with the movement of major storm areas over the earth's surface exerts a dominant influence in determining the incidence of rheumatic attacks. Attacks of rheumatic fever and rheumatic cardiac disease occur from ten to twenty times more often in the worst areas of the storm zones than in the calm warmth of the tropics. In northern countries their difference in incidence between winter high and summer low is almost as striking as is the regional one. Those afflicted in the North usually show improvement in symptoms on migration to subtropical regions. Such improvement is soon lost when they again experience the northern winter and early spring weather. For lasting benefit they must forego living in the stormy North and take up permanent residence in the subtropics. The more even seasonal distribution of attacks of rheumatic fever between summer and winter in Buenos Aires, reported by Coburn, is of some significance in establishing the etiologic importance of atmospheric instability, especially when such storminess is associated with lower temperatures. When a permanent change of residence is possible the choice region from a climatic point of view in this country is the southern parts of New Mexico, Arizona and California.

### Journal-Lancet, Minneapolis

58: 427-464 (Oct.) 1938

- The Value of Roentgen Rays in Diagnosis. C. G. Sutherland, Rochester, Minn.—p. 427.  
Treatment of Gonorrhea with Sulfanilamide. D. E. Ellison, Minneapolis.—p. 433.  
The Needs of the Tuberculous. H. E. Hilleboe, St. Paul.—p. 440.  
\*Pulmonary Embolism: Report of Fifty-Four Cases. P. J. Breslich, Minot, N. D.—p. 445.  
Obstetric Syphilis. E. D. Plass, Iowa City.—p. 449.

**Pulmonary Embolism.**—Breslich reports fifty-four cases of pulmonary embolism that were found in the 457 postmortem examinations performed from June 1932 to December 1936. Of these, thirty-seven were in medical and seventeen in surgical patients. In 51 per cent of the cases the emboli were associated with lung infarcts. Only three of the thirty-seven patients in the medical group were 40 years of age or less, twelve of whom were definitely obese, eighteen of normal weight and seven emaciated. The leukocyte counts were elevated in twenty-six instances, also there was some degree of fever during the period of hospitalization. Fever and leukocytosis were present in four patients with recent myocardial infarcts and in two with an inoperable carcinoma. In twelve there were obvious suppurative lesions. In the remaining eight instances the occurrence of fever and leukocytosis prior to infarction of the lung or hypostatic bronchopneumonia was not explained. In only five of the thirty-seven cases were the hearts considered normal at postmortem examination. There were only three sudden deaths due to massive pulmonary embolism in the entire group. In twenty-one of the thirty-seven medical cases lung infarcts were present and associated with small emboli, in nineteen of which there was unmistakable postmortem evidence of cardiac decompensation. Venous thrombi which indicated a possible source of pulmonary emboli were discovered in twenty-six instances. Most of the venous thrombi caused no local symptoms, and in only five cases were they recognized before death. Other recognized sources of emboli were thrombi in the left cubital vein, right subclavian vein and veins of the left thigh in one instance

each. In twenty-one patients with pulmonary infarcts, clinical signs were sufficient to make a diagnosis only eleven times. Several of these were thought to be instances of bronchopneumonia before death. In the remaining ten cases pulmonary infarcts caused no symptoms and were discovered only at post-mortem examination. Of the seventeen surgical patients who died following operation thirteen were definitely obese, two of normal weight and two emaciated. Twelve of the patients were more than 50 years of age, four were 40 years of age or less and one was in the fifth decade. In nine there was either a marked hypertrophy of the myocardium of the left ventricle suggesting previous arterial hypertension or serious coronary artery sclerosis or both. There was one instance of acute myocarditis. In seven cases the heart was considered normal at postmortem examination. Lung infarcts were present in seven, and in five of them there were pathologic changes in the heart resulting from arterial hypertension and coronary artery sclerosis. Thirteen patients died suddenly of massive pulmonary embolism, during convalescence from operations involving the abdomen, pelvis or abdominal wall. Death occurred from two to 111 days after operation, but there were eleven deaths in the first three postoperative weeks. In six of these thirteen cases thrombi were discovered in the pelvic or leg veins. In the other seven cases blood clots became detached from the lining of the veins in their entirety and left no trace of their source. In seven of the seventeen surgical cases extensive, acute or chronic inflammatory lesions other than terminal bronchopneumonia were present at the time of death. Three of the seven showed hypertensive cardiovascular disease with sclerosis of the coronary arteries, while in the others the hearts were normal. Three of the seventeen patients had carcinoma, and in one of these acute myocarditis was discovered at necropsy. In the other two the hearts were normal.

### Journal of Pediatrics, St. Louis

13: 455-618 (Oct.) 1938

- Tonic Neck Reflex in the Human Infant: Morphogenetic and Clinical Significance. A. Gesell, New Haven, Conn.—p. 455.
- \*Use of Honey as Carbohydrate in Infant Feeding. F. W. Schlutz and Elizabeth M. Knott, Chicago.—p. 465.
- Statistical Studies on Prematurity: I. Incidence of Prematurity and Effect of Certain Obstetric Factors. C. H. Peckham, Baltimore.—p. 474.
- Id.: II. Mortality of Prematurity and Effect of Certain Obstetric Factors. C. H. Peckham, Baltimore.—p. 484.
- Influence of Metabolism on Teeth. J. O. McCall and Frances Krasnow, New York.—p. 498.
- Biophotometer as Test for Vitamin A Deficiency. C. E. Snelling, Toronto.—p. 506.
- New Tuberculin Patch Test. W. D. Steward, Chattanooga, Tenn.—p. 510.
- Relation of Intestinal Bleeding to Heterotopic Gastric Mucosa and Ulceration in Meckel's Diverticulum. A. L. Abrams, New York.—p. 513.
- Nervous System in Acrodynia: Review of Literature and Report of Case. A. J. Lubin and H. K. Faber, San Francisco.—p. 515.
- \*Sulfanilamide in Treatment of Gonorrheal Ophthalmia in Children. M. W. Michels, Detroit.—p. 527.
- Rupture of Liver in the Newborn Infant. H. B. Silver, Newark, N. J.—p. 542.
- Congenital Absence of Teeth: Absent Deciduous and Permanent Right and Left Central and Lateral Incisors and Canines of Lower Jaw. J. L. Stein and A. Gerber, Brooklyn.—p. 547.
- Methyl Salicylate Poisoning in an Infant: Report of a Patient with Partial Necropsy. A. Eimas, Bridgeport, Conn.—p. 550.

**Honey in Infant Feeding.**—Schlutz and Knott studied the suitability of honey as the source of carbohydrate for ten healthy male infants aged 1 month or less. The period of observation continued until the infants were 6 months old. Formulas for all infants were restricted to either evaporated or dried milk and carbohydrate, with additional supplements of pure vitamin or mineral solutions. The general well being of the infant, the number of stools daily and weight gains have been used to determine the value of honey in regular feedings. Besides these criteria, blood sugar tolerance studies have been employed to contrast the response to honey with that resulting from administration of other common sources of carbohydrate. It was found that honey is easily digested, being absorbed more rapidly than most sugars during the first fifteen minutes after ingestion. It is well tolerated by the infant and does not cause diarrhea. It may facilitate weight gains, since there was a slight tendency for greater average gains daily to occur on lower calory intakes when honey was included in the formulas. It appears that honey should be recommended for wider use in diets of infants.

**Sulfanilamide in Gonorrheal Ophthalmia.**—Michels used sulfanilamide orally in the treatment of fifteen cases of proved gonorrheal ophthalmia. Sulfanilamide was given on the approximate dosage basis of 1 grain (0.065 Gm.) per pound of body weight daily combined with equal amounts of sodium bicarbonate. The average hospital duration of the fifteen patients was 5.8 days. The ages of the patients varied from 5 days to 3 years. Of these, two showed corneal involvement; perforation did not result after sulfanilamide was started. Six of the group showed bilateral involvement. None of the complications attributed to sulfanilamide were observed in these patients. In the two years prior to the use of sulfanilamide in the thirty-two similar cases treated for gonorrheal ophthalmia by the usual methods the average hospital duration was 28.5 days. Corneal involvement occurred in two cases, two going on to perforation. Eighteen patients had involvement of both eyes. Four other patients treated by sterile milk were hospitalized for an average of 16.5 days; none of these showed corneal involvement.

### Maine Medical Journal, Portland

29: 203-234 (Oct.) 1938

- Care of the Indigent Sick in the State of Maine. G. W. Leadbetter, Augusta.—p. 203.

### Medical Annals of District of Columbia, Washington

7: 307-334 (Oct.) 1938

- Asphyxia of the Newborn. H. R. Litchfield and J. S. Beilly, Brooklyn.—p. 307.
- Progress, Science and the Mind: A History of Saint Elizabeths Hospital. J. P. H. Murphy, Washington.—p. 313.
- Cranial Osteomyelitis: Report of Two Unusual Cases. J. Rose, M. M. Schapiro and E. P. McLarney, Washington.—p. 323.
- Barium Enema as Most Accurate Procedure in Diagnosis of Pathology of the Colon. C. Moore, Washington.—p. 325.

### Michigan State Medical Society Journal, Lansing

37: 861-956 (Oct.) 1938

- Problems of Medical Care Facing the Medical Profession. H. Cook, Flint.—p. 879.
- The Early Treatment of Mental Disorders. W. Overholser, Washington, D. C.—p. 883.
- The Lie Detector: Its History and Development. J. A. Larson, Detroit.—p. 893.
- The Medicolegal Aspects of the Polygraph or "Lie Detector." L. S. Selling, Detroit.—p. 897.
- Desensitization Treatment in Skin Diseases. G. L. Waldbott, Detroit.—p. 901.
- Management of Circulatory Failure. L. M. Warfield, Milwaukee.—p. 905.
- Punch Card Code for Classification of Craniocerebral Injuries. F. Schreiber and A. Nielsen, Detroit.—p. 909.
- Palliative Surgery in Carcinoma of the Stomach. C. F. Vale, Detroit.—p. 912.
- Chronic Encephalitis. R. N. De Jong, Ann Arbor.—p. 916.
- \*Acute Yellow Atrophy of the Liver Caused by Poisonous Mushrooms: Report of Cases. J. H. Ahronheim, Jackson.—p. 921.

**Atrophy of Liver from Mushrooms.**—Ahronheim reports a case of acute yellow atrophy of the liver due to the ingestion of poisonous mushrooms (*Amanita phalloides*). Besides the changes in the liver, a marked hemorrhagic diathesis and degenerative fatty changes in the kidneys and myocardium were found at necropsy. The complete recovery of the patient's wife, in spite of more severe symptoms, indicates that in her case the principal effect of the toxic substance was outside the liver, probably in the intestinal tract only.

### Military Surgeon, Washington, D. C.

83: 193-272 (Sept.) 1938

- Medical Units in the National Guard. A. H. Blanding.—p. 193.
- Management of Eye Wounds at the Front. R. A. Fenton.—p. 195.
- Penetrating Wounds of Chest, with Report of Case, Gunshot Wound. J. R. Weisser.—p. 202.
- Control of Venereal Disease in the United States Army. W. W. Vaughan.—p. 208.
- Saint Elizabeths Hospital. E. H. Parsons and Winfred Overholser.—p. 227.
- The First Annual Military Medicodental Training Course for Medical Department Reserve Officers, Chicago, Ill. C. C. MacLane.—p. 235.
- \*Simple Treatment for Epidermophytosis of Feet. J. A. Meleady.—p. 250.

**Treatment for Epidermophytosis of Feet.**—In the treatment of epidermophytosis of the feet Meleady instructs his patients not to use soap and water for bathing them but olive oil during the period of treatment. The patient soaks his feet for twenty minutes in a solution containing two tablespoonfuls

of sodium hyposulfite to 2 quarts of water. Following this his feet are thoroughly dried and then exposed for a period varying from five to seven minutes to the actinic rays at a distance of about 18 inches. While the feet are thus exposed the toes are separated so that the rays can penetrate thoroughly into the spaces between and under them. At the completion of the treatment, the feet are thoroughly dusted with a carefully compounded semianhydrous dusting powder of desiccated sodium thiosulfate enhanced by the synergistic action of thymol and an acceptable base of starch and boric acid with oil of absinthium as a deodorant and the patient is instructed to put on clean socks. Prior to putting on shoes, preferably new, the powder is dusted freely over their entire inner surfaces. The patient is then instructed that prior to retiring he is to remove the socks which he had worn during the day, dust the feet thoroughly with the powder and put on a pair of clean socks and wear them during the night. In the morning he is to change his socks for a clean pair and have another pair with him when he reports for treatment. This routine is followed daily. The average time consumed for the treatment is about two weeks. Twenty-two patients have been treated and all have responded favorably.

### Minnesota Medicine, St. Paul

21: 671-744 (Oct.) 1938

- The Social Side of Medical Progress. H. W. Haggard, New Haven, Conn.—p. 671.  
Medicine and the Law. J. M. Gallagher, Waseca.—p. 677.  
Professional Cooperation in the Public Interest. S. B. Houck, Minneapolis.—p. 680.  
Herman M. Johnson: Past and Present Medical Problems. E. A. Benson, St. Paul.—p. 684.  
Fractures—General Principles. C. Jacobson, Chisholm.—p. 688.  
Recognition and Treatment of Refractive Errors in Children. E. Jackson, Denver.—p. 692.

### New England Journal of Medicine, Boston

219: 503-546 (Oct. 6) 1938

- \*The Oral Aspects of Diabetes Mellitus. A. Rudy and M. M. Cohen, Boston.—p. 503.  
The Maximal Temperature of Expired Air as a Rapid Measure of Human Body Temperature. F. G. Benedict, Cornelia G. Benedict, R. C. Lee and Helen B. Lee, Boston.—p. 509.  
Chronic Arthritis of the Shoulder: Diagnosis and Treatment. J. G. Kuhns, Boston.—p. 516.  
Treatment of Chronic Bronchial Asthma. E. A. Brown, Boston.—p. 520.  
Progress in Nutrition. F. L. Burnett, Boston.—p. 524.

**Oral Aspects of Diabetes Mellitus.**—Rudy and Cohen studied the oral manifestations of 403 diabetic patients. Of the patients studied, 138 were advanced in years, presenting edentulous mouths and as a result no dental treatment was necessary. Among the remaining 265 were four children and three young adults who had diabetes of long standing. In six of these the teeth were excellent from the functional point of view, with comparatively few carious teeth and no abnormal tartar formation. In the younger children the eruption of the permanent teeth was normal and in the right relation to their ages. Two of the children who presented normal mouths clinically had incipient parodontal lesions. The seventh patient, a young man with severe diabetes, receiving 68 units of insulin a day, had many carious teeth. He had gingival and parietal abscesses on two occasions, when the diabetes became uncontrolled because of dietary indiscretion or inadequate insulin dosage. As a general rule the adult, dentulous, medically controlled patients who were examined presented mouths which were unclean, owing to lack of oral hygiene, with heavy deposits of both supragingival and subgingival calculus. Roentgenographically and clinically this group has a high incidence of diffuse alveolar atrophy. This is particularly true of the younger age group (25 to 45), in which diffuse alveolar atrophy is not generally attributed to local causes. Patients with acute or inadequately treated diabetes present a characteristic oral symptomatology. It is manifested clinically in the gingival papillae, which become markedly swollen and tender and bleed profusely on the slightest pressure. These patients also present loosening of the teeth. This is associated with pain, especially on percussion. With control of the diabetes the acute inflammatory condition of the gingiva subsides, the loosened teeth become fixed and pain on percussion disappears. Extraction of teeth in the inadequately controlled diabetic patient results in a prolonged period of sup-

uration and pain. Local treatment without attention to the diabetes is futile. Infected teeth may aggravate the diabetes and should therefore be removed. Extraction of teeth should be carried out only on controlled diabetic patients and under the supervision of a physician. Neglect may result in serious complications.

### New Orleans Medical and Surgical Journal

91: 163-210 (Oct.) 1938

- Insulin Allergy: Report of Severe Case with Successful Desensitization. A. A. Herold, Shreveport, La.—p. 163.  
Causes of Blindness in Louisiana: Review of 700 Cases. H. F. Brewster, New Orleans.—p. 166.  
The Eye and Ear in Industrial and Social Life. D. Bean, Shreveport, La.—p. 173.  
The Symptoms, Diagnosis and Treatment of Carcinoma of the Rectum and Sigmoid Colon. B. C. Garrett and L. L. Davidge, Shreveport, La.—p. 177.  
Neoplasia of Testes. F. L. Loria, New Orleans.—p. 187.  
Banana and Banana Powder Therapy in Diarrheal Diseases of Infants and Young Children. E. A. Socola, New Orleans.—p. 192.  
Urinary Infections and Their Management. I. B. Rougon, Shreveport, La.—p. 196.

### Oklahoma State Medical Assn. Journal, McAlester

31: 333-366 (Oct.) 1938

- Analysis of 1,514 Inguinal Herniotomies. W. P. Fite, Muskogee.—p. 333.  
Surgical Diseases of Gallbladder and Bile Ducts. D. L. Garrett, Tulsa.—p. 338.  
Actinomycosis in Man: Case. W. H. Bailey, Oklahoma City.—p. 339.  
Thoracoplasty in Treatment of Tuberculosis. R. M. Shepard, Tulsa.—p. 342.  
Acute Infective Laryngotracheobronchitis. C. M. Pounders, Oklahoma City.—p. 344.

### Public Health Reports, Washington, D. C.

53: 1817-1854 (Oct. 14) 1938

- Effect of Sodium Selenite and Selenate on Oxygen Consumption of Mammalian Tissues. C. I. Wright.—p. 1825.  
Assay of Urine in Canine Blacktongue by the Use of Shigella Paradyenteriae (Sonne). H. F. Fraser, N. H. Topping and W. H. Sebrell.—p. 1836.

### Western J. Surg., Obst. & Gynecology, Portland, Ore.

46: 513-566 (Oct.) 1938

- Smooth Muscle Tumors of Stomach: Review of Literature with Report of Case (Leiomyosarcoma). L. Chaffin, Los Angeles.—p. 513.  
Giant-Cell Tumor of the Patella: Case Report. R. B. Dillehunt and E. G. Chuinard, Portland, Ore.—p. 525.  
Multiple Ectopic Parathyroid Adenomas. G. S. Fahrni, Winnipeg, Man.—p. 528.  
Amimia—Unilateral Fascial Emotional Palsy, as Sign of Destructive Contralateral Thalamostriate Lesions. A. J. McLean, Portland, Ore.—p. 533.  
Mesenteric Infarction Due to Thrombosis of Mesenteric Vessels Causing Chronic Intestinal Obstruction: Case Report. T. Shinkawa and N. Mori, Nagoya, Japan.—p. 545.  
Carcinoma of Breast with Krukenberg Type Metastasis: Report of Case. C. P. Larson, Tacoma, Wash.—p. 550.  
\*Blood Calcium: Its Relation to Certain So-Called Angiospastic Conditions. G. F. Norman, San Francisco.—p. 553.

**Blood Calcium and Angiospasm.**—In 1934 Norman described a peculiar relationship between mild hypocalcemia and idiopathic migraine including the report of a few cases exhibiting convulsive seizures. Vascular spasm was accepted to explain the phenomena observed. This concept has now been extended to designate a preexisting localized vascular irritability probably operative through the sympathetic nervous system and inhibited normally by an adequate level of ionized calcium in the blood. A few patients exhibiting the Raynaud complex in moderate degree, either in association with migraine or independent of this condition, could be segregated into the same group. Close questioning will reveal the frequency of blanching fingers and paresthesias in a large group of patients and the association with migraine is quite striking. The author's series now includes about 200 patients from private practice complaining of biliousness or sick headache with nausea and vomiting, and the results have justified the employment of viosterol to raise the blood calcium. A large percentage of cures has been obtained with no other form of treatment. In the small ratio not completely relieved, a diminution of both frequency and severity of the attacks has occurred, frequently persisting for six months after interruption of the therapy.



## FOREIGN

An asterisk (\*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

## Australian J. Exper. Biol. &amp; M. Science, Adelaide

16: 193-274 (Sept.) 1938. Partial Index

- Myxoma and the Shope Fibroma: V. Myxoma in Fibroma-Immune Rabbit, with Summary of Present Knowledge of Relationship Between Myxoma and Fibroma Viruses. E. W. Hurst.—p. 205.  
Tissue Culture of the Rickettsia of Q Fever. F. M. Burnet.—p. 219.  
Infection of Central Nervous System by Louping Ill Virus: Investigation by Quantitative Egg Membrane Technic. F. M. Burnet and Dora Lush.—p. 233.  
The Polynuclear Count in the Australian Aborigine. B. Macgrath.—p. 241.  
Susceptibility of the Dog to Q Fever. E. H. Derrick, D. W. Johnson, D. J. W. Smith and H. E. Brown.—p. 245.  
Liberation of Histamine by Staphylococcus Toxin and Mercuric Chloride. W. Feldberg and C. H. Kellaway.—p. 249.  
Influenza Virus on the Developing Egg: VIII. Comparison of Two Antigenically Dissimilar Strains of Human Influenza Virus After Full Adaptation to the Egg Membrane. F. M. Burnet and Dora Lush.—p. 261.

## British Journal of Dermatology and Syphilis, London

50: 487-574 (Oct.) 1938

- The British Journal of Dermatology and Syphilis, 1888-1938: A Retrospect J. M. H. Macleod.—p. 487.  
Looking Backward. J. H. Sequeira.—p. 498.  
Celebrated British Dermatologists of the Past Fifty Years. E. Graham-Little.—p. 503.  
Dermatomyositis and Poikiloderma Atrophicans Vascularis: Clinical and Histologic Comparison. G. B. Dowling and W. Freudenthal.—p. 519.  
Emulsifying Bases in Dermatology. P. B. Mumford.—p. 540.

## British Journal of Radiology, London

11: 641-704 (Oct.) 1938

- Epidermal Tumors of Skin. I. G. Williams.—p. 641.  
Carcinoma of Cecum Causing Intussusception, with Special Reference to Roentgenologic Features: Case. A. G. G. Melville.—p. 649.  
\*Radiotherapeutic Treatment of Certain Granulomas. R. McWhirter.—p. 664.  
Peptic Ulcer of Greater Curvature of the Stomach. F. S. P. van Buchem.—p. 667.  
Symptomless Pericarditis: Report of Two Cases. E. L. Rubin and M. H. Pappworth.—p. 671.  
X-Ray and Gamma-Ray Protective Values of Building Materials. G. W. C. Kaye, W. Binks and G. E. Bell.—p. 676.  
Existence of Critical Intensity. W. H. Love.—p. 686.

**Roentgen Treatment of Granuloma.**—McWhirter divides the granulomas into three groups: actinomycosis in which the diagnosis is established by demonstrating the ray fungus in the discharge, granuloma of the vulva and anus associated with venereal disease, and a group of granulomas in which a causal organism cannot be determined. He has encountered fifteen cases of actinomycosis in the last three years. In the earlier cases treatment with x-rays was generated at 180 kilovolts and filtered by 0.7 mm. of copper. During the last eighteen months a still harder quality beam (250 kilovolts and Thoraeus filter) has been employed. Daily treatments of about 100 roentgens have been given (the dose is varied according to the site treated, the area of the field and the age of the patient) over a prolonged period and the dose to the lesion carried as high as 4,000 roentgens. The author believes that daily treatments are superior to weekly treatments and considers high dosage advisable in order to prevent recurrence of the suppuration. A hard quality beam would also seem advisable, as many of the lesions extend to a considerable depth. Drainage may be necessary if there is much necrotic debris. Of the lesions treated, seven of the eight affecting the face and neck have healed. The unhealed one is recent. Of the four abdominal lesions, three have healed and there is a small discharging sinus in one which is gradually closing in. Healing has occurred in one of the two cases in which the wall of the chest was involved. The condition has soundly healed in the case in which the buttock was involved. All the patients are alive, in twelve the sinuses have healed completely and in the remaining three there is marked improvement. The lesions of anal and vulvar granulomas are very sensitive to x-rays and may disappear rapidly with a single dose of 300 roentgens. Occasionally this requires to be repeated after an interval of a week. Seven patients with such granulomas have been treated and all are well. Granulomas of

unknown origin are serious; four of the seven patients with this type of granuloma are dead. Two others are in poor general health. The seventh patient is fit and well. The mouth, pharynx or neck has been primarily involved in all these cases. The lesions resemble malignant conditions but lack the characteristic induration and are often extensive while yet remaining superficial. In other cases the ulceration has been deep and microscopic examination is necessary to exclude malignant disease. As a rule, the general health of the patient is poor. No fungus has been found in any of the cases. The clinical appearance and history, however, suggest that the condition is produced by a fungous infection.

## British Journal of Urology, London

10: 219-322 (Sept.) 1938

- Renal Fusion; Urographic Data and Their Clinical Significance. W. F. Braasch and H. J. Hammer.—p. 219.  
"Pseudo-Uremia" of Patients with Prostatic Hypertrophy: The Nephrogenous Acidosis. H. Retlev-Abrahamsen and V. Aalkjaer.—p. 231.  
Regarding the Cure of Prostatic Hypertrophy with Synthetic Testicular Hormones. A. Oberholtzer.—p. 237.

## British Medical Journal, London

2: 729-772 (Oct. 8) 1938

- The Modern Decline of Breast Feeding. J. C. Spence.—p. 729.  
The Spread of Streptococcal Disease. W. H. Bradley.—p. 733.  
\*Glucose Tolerance Curves in 500 Obese Cases. D. Embleton.—p. 739.  
Corneal Transplantation: Results of a Series of Fifty-Six Operations on Forty-Eight Eyes. J. W. T. Thomas.—p. 740.  
\*Vitamin C in Treatment of Whooping Cough. D. Gairdner.—p. 742.

**Dextrose Tolerance Curves and Obesity.**—Embleton reviewed the 500 cases (242 in males and 258 in females) of obesity in which a dextrose tolerance curve was made during the last fifteen years. No examples of gross endocrine disturbance, with the exception of diabetes, are given. It is possible that the series does not represent a fair sample of the obese population of the country, as the patients came from the better-off classes. Only a small proportion have presented themselves because sugar has been found in the urine. The most striking result from the analysis is the difference between the obese of the two sexes. The men show a total of 73 per cent high curves for all ages, whereas the women show only 35 per cent of high curves. This difference in response to dextrose is still more pronounced if the percentage of high curves is plotted for the various decades. In men up to the age of 35 years the percentage of high dextrose tolerance curves is below 30. After this age a sudden rise occurs, so that between 35 and 45 nearly 80 per cent of obese men show a high dextrose tolerance curve, after which this high level is maintained up to the age of 65 and beyond. In obese women, on the other hand, the percentage of high curves remains low until a decade later, 45 years. The rise when it occurs is less sharp, the highest percentage of high curves (70) not being reached until the decade 55 to 65 years. A striking difference is often evident in the postmortem room. An obviously obese woman may be encased in layers of fat, but within this the body appears healthy and the muscles a bright red and not infiltrated with fat. In the male this is rare; if it ever occurs the musculature is heavily infiltrated with fat. A man is more likely to have a high blood sugar curve if he is 50 per cent overweight than if he is even less than 10 per cent overweight. A woman 60 per cent overweight is not more likely to show a high blood sugar curve than one only 10 per cent overweight.

**Vitamin C in Treatment of Whooping Cough.**—Gairdner used large doses of vitamin C in the treatment of twenty-one children with whooping cough and twenty others served as controls. They were seen as outpatients once a week. Only those patients were included in the series who satisfied one or more (in the majority at least two) of the following diagnostic criteria: (1) Haemophilus pertussis recovered from the cough plate, (2) a typical paroxysmal cough witnessed and (3) a suggestive history combined with the presence of either a sublingual ulcer or a marked lymphocytosis. The dosage adopted was first week 200 mg. daily, second week 150 mg. and third and subsequent weeks 100 mg., given in divided doses. The illness in the treated patients lasted an average of thirty-five days as compared with forty-one days in twenty control patients, a difference which lies within the limits of statistical error. The average

rate of weight gained was practically the same in the two groups. These figures are in keeping with the general clinical impression that there was no striking difference in the course of the disease in the two sets of cases, and the assertion of Ormerod and UnKauf that the paroxysmal period of the disease is shortened "from a matter of weeks to a matter of days" was not confirmed.

### Indian Medical Gazette, Calcutta

73: 513-584 (Sept.) 1938

- Study of Antituberculosis Activities in the West, with Some Suggestions for a Campaign Against Tuberculosis in India. C. Frimodt-Møller.—p. 513.  
Campaign Against Tuberculosis in Italy. T. J. Joseph.—p. 522.  
Antituberculosis Work in Bengal. A. C. Ukil.—p. 525.  
Seriousness of Tuberculosis in India as Shown by Study of Incidence and Type. P. V. Benjamin.—p. 540.  
Deductions from Experience in Tuberculosis Ex-Patients' Colony in India. P. V. Benjamin and R. M. Barton.—p. 545.  
Tuberculosis in the Zenana. Rose A. Riste.—p. 551.  
Role of Solariums in Antituberculosis Work. B. Jayaram and A. K. Sheriff.—p. 557.  
Methods of Destruction of Tubercle Bacilli in Sputum for Use in Indian Homes, with Some Experiments. R. M. Barton.—p. 559.

### Irish Journal of Medical Science, Dublin

No. 153: 597-644 (Sept.) 1938

- \*Clinical Diagnosis of Congenital Heart Disease. P. T. O'Farrell.—p. 597.  
Tuberculosis of the Male Genital Tract. E. D. McCrea.—p. 614.  
Analeptics and the Bragg-Paul Pulsator. R. H. Micks.—p. 629.

**Congenital Heart Disease.**—O'Farrell lists the following criteria as helpful in the diagnosis of congenital cardiac disease: 1. A clear history of cardiac disease existing from birth or early infancy (in the absence of infection) is suggestive, but it should be remembered that many cases of congenital cardiac disease do not present recognizable features until fairly well on in life. 2. Murmurs and thrills heard and felt at an unusual situation, and not conforming to those produced by acquired disease as regards both the area of maximal intensity and conventional direction of propagation, deserve close attention. When murmurs originate from congenital lesions they tend in adult patients to be constant throughout life, but in children murmurs may sometimes undergo variation and on rare occasions disappear. 3. Cyanosis is a prominent feature only in the cyanotic forms of congenital cardiac disease. Cyanosis in congenital cardiac disease is due to hindrance of access of the blood to the lungs and the presence of a venous-arterial shunt whereby some of the venous blood is short circuited from the pulmonary into the general circulation. The mechanism of congenital cyanosis nearly always implies the presence of complicated malformations of the heart. The cyanosis is not an expression of congestive failure except as a terminal event, and therefore the concomitant signs and symptoms of congestive failure are lacking. Cyanosis in congenital cardiac disease may be permanent, transient, delayed or paroxysmal, depending roughly on the severity of the lesion; therefore cyanosis is of assistance as a means of assessing prognosis. 4. Polycythemia is seldom if ever seen in the acyanotic group of cases, and it is not a constant feature in the cyanotic group. 5. Clubbing of the fingers and toes is an important sign. The degree of clubbing is roughly proportional to the duration and severity of cyanosis; therefore it is seen most characteristically in well marked chronic cyanotic cases. 6. Dyspnea with respiratory embarrassment varies according to the severity of the lesion. Dyspnea is sometimes paroxysmal and, as in paroxysmal cyanosis, recovery is often rapid. 7. Developmental defects in other parts of the body are not infrequently found in association with congenital cardiac lesions. 8. Subacute bacterial endocarditis occurs frequently. It is more common in the acyanotic group, probably because these patients live longer. 9. Juvenile hypertension is of diagnostic significance only in coarctation of the aorta. 10. X-ray examinations are of great importance provided the observations are correlated with the other clinical manifestations. Many congenital lesions show abnormal alteration of the cardiac outline when viewed under the screen. 11. Electrocardiography will only verify or refute the accuracy of a clinical diagnosis, chiefly in respect to deviation of the electrical axis.

### Journal of Mental Science, London

84: 589-892 (Sept.) 1938

- The Low-Rate Private Patient and Some Changes. J. R. Gilmour.—p. 596.  
Disturbances of Somatic Functions in Catatonia with Periodic Course and Their Compensation. R. Gjessing.—p. 608.  
Influence of Pharmacologic Shocks on the Psychoses. M. Sakel.—p. 626.  
Observations on Convulsion Therapy with Triazol. A. Walk and W. Mayer-Gross.—p. 637.  
Range of Mental Reaction States Influenced by Cardiazol Convulsions. L. C. Cook.—p. 664.  
Psychologic Aspects of Insulin Shock Therapy: Psychosomatic Study. E. Larkin.—p. 668.  
Insulin and Cardiazol: Experiences of the Combined Method. L. W. Russell.—p. 672.  
Dangers and Emergencies of Insulin Therapy of the Psychoses. L. A. Finiefs.—p. 678.  
Some Genetic Problems in Mental Deficiency. L. S. Penrose.—p. 693.  
Consanguinity and Mental Disorder. T. A. Munro.—p. 708.  
Technic and Complications of Insulin Therapy. S. W. Gillman and D. N. Farfitt.—p. 718.  
Cardiazol Treatment of Schizophrenia. A. Harris.—p. 735.  
Neurologic Manifestations Seen During Cardiazol and Insulin Treatments. D. Blair.—p. 776.  
Electro-Encephalogram in Schizophrenia. J. F. MacMahon and W. G. Walter.—p. 781.  
Some Observations on Vitamin C Deficiency in Acute Mental Disorder. F. T. Thorpe.—p. 788.  
\*Homesickness and Immigrant Psychoses: Austrian and German Domestic Servants the Basis of Study. I. Frost.—p. 801.

**Nostalgia and Immigrant Psychoses.**—In the space of six years Frost saw forty Austrian and German domestic servants suffering from mental disorders. Homesickness combined with loneliness and exhaustion comprise the principal etiologic factors producing psychoses among immigrants. Hereditary elements do not figure prominently. Mistakes of identity are common and illusions of resemblance appear to follow the stratifications peculiar to primitive notions of kinship. The forms of mental disorder encountered in the present series of cases comprise acute confusional states, acute schizophrenic conditions, paraphrenia and involutional forms. Rarely reactive depressive and twilight states occur. Endogenous manic-depressive insanity is rarer still. Bodily reactions may be seen in all the foregoing forms; loss of appetite, toxemia and vegetative-nervous changes are most common and are most likely to be found in the acute confusional and acute schizophrenic types of disorder.

### Journal of Tropical Medicine and Hygiene, London

41: 277-292 (Sept. 1) 1938

- Smooth and Rough Forms of *Monilia Tropicalis* Cast in Sputum of the Same Patient. A. Castellani.—p. 277.  
Hereditary Transmission of Lymphogranulomatosis Venerea. W. E. Coult and Olga Monetta.—p. 279.  
Trypanosomiasis Gambiensi: Some Observations in Uganda and Their Bearing on Prophylaxis. A. A. F. Brown.—p. 281.

41: 293-308 (Sept. 15) 1938

- Favorite Sites of Schistosomes and Consideration of Their Destruction in Stock. F. G. Cawston.—p. 293.  
\*Pellagroid Beriberi (Dermoberiberi). A. Castellani.—p. 294.  
Trypanosomiasis Gambiensi: Some Observations in Uganda, and Their Bearing on Prophylaxis. A. A. F. Brown.—p. 296.

**Pellagroid Beriberi.**—In countries in which beriberi and pellagra are endemic, cases are encountered in which symptoms of the two diseases are present concomitantly. To cover these cases Castellani introduces the term "dermoberiberi" or "pellagroid beriberi." In a typical case of pellagroid beriberi the following features are present: 1. The typical symptoms of beriberi present are weakness and paresis of the lower extremities, loss of the knee jerk, stepping gait, pain in the calves on pressure, patches of anesthesia or hyperesthesia, slight pretibial edema, normal pupils and normal urine. 2. Some of the symptoms of pellagra are chronic roughening and pigmentation of the exposed skin, but at times also of unexposed parts of the body and around the anus. At times stomatitis and angular stomatitis may be present. 3. Keratosis pilaris-like eruption, with numerous, often nonpruriginous, horny papules, which give a feeling of a nutmeg grater, are mostly found on the extensor parts of the legs, thighs and arms (the eruption may be limited to the buttocks and lateral parts of the thighs). This is a well known feature of avitaminosis A. These cases are probably due to a pluriavitaminic deficiency.

## Annales de Médecine, Paris

44: 165-312 (Oct.) 1938

Septicopyemia with *Bacillus Funduliformis*. A. Lemierre, J. Reilly and A. Laporte.—p. 165.

Septicemia with *Bacillus Fragilis*. Mme. Ternois.—p. 201.

Septicemias with *Streptobacillus Moniliformis*. M. Morin.—p. 219.

\*Clinical Study of Forty-Eight Cases of Septicemia with Hemolytic *Streptococcus*. J.-A. Lièvre.—p. 245.

Several Observations on Colibacillemia. R. Roch.—p. 271.

Study of Septicemia with Diphtheria Bacilli with Endocarditis Appearing in Course of Diphtherial Angina. P. Lenti and Mlle. S. Wirz.—p. 293.

**Septicemia with Hemolytic *Streptococcus*.**—Lièvre bases this report on forty-eight cases which were observed at the clinic for infectious diseases at the faculty of medicine in Paris during the years 1933, 1934 and 1935. He says that in the majority of cases the streptococcic septicemia is not a primary disease; it usually is a secondary manifestation in a pathologic process which indicates clearly the way by which the pathogenic agent was introduced into the organism. In only two of the forty-eight cases was the cause not clear. In localized streptococcic infections, such as erysipelas, the streptococcus is likely to pass into the blood. Eruptive fevers likewise may become complicated by streptococcic septicemia. The author observed cases after measles which, however, were complicated with streptococcic otitis or sinusitis. The infections of the middle ear have an important part and tonsillar processes may assume a role. Discussing the symptomatology of septicemia with hemolytic streptococci, the author takes up the mode of onset, the fever curve, the general condition, the cutaneous symptoms and the involvement of the internal organs. In his discussion of the treatment he first cites mortality statistics, showing that mortality rates have been known to reach 90 per cent. In his own material, twenty-four of forty-four patients died, a mortality of 54.5 per cent. Following remarks about general measures, particularly the diet, the author says that the removal of the focus of infection is an important factor in the treatment. He says that the results obtained with serotherapy vary greatly in different reports. The experiences at his clinic have not been encouraging, for of fourteen patients subjected to serotherapy only three recovered. About blood transfusions he says that generally the effect was not clear; it was not harmful and it even seemed to improve to a certain extent the general condition and the anemia. In four cases the blood transfusion had a definite effect on the evolution of the septicemia. This effect became manifest in a rapid decrease in the temperature. The clinical histories of these cases indicate that sometimes blood transfusion may effect a sudden improvement in streptococcic septicemia.

## Gynécologie et Obstétrique, Paris

38: 161-240 (Sept.) 1938

Puerperal Abscess of Uterus. R. Démarez.—p. 161.

\*Treatment of Toxemia or Toxicosis of Pregnancy with Progesterone. H. van der Hoeven.—p. 172.

Sterilization of Females of White Mice by Instillation of Estrogen into Vagina. A. I. Kroupsky and A. A. Bloonskaia.—p. 182.

Surgical Treatment of Uterine Retrodeviation. D. Dumbadze.—p. 186.

Intramural Pregnancy. S. I. Stern.—p. 193.

**Progesterone in Toxicosis of Pregnancy.**—After calling attention to the increased urea content of the blood in women with pregnancy toxicosis and to the effect of thyroid on this condition, van der Hoeven says that he tried estrogen without satisfactory results. Later he tried progesterone, the hormone of the corpus luteum, and obtained better results. In this connection he points out that an article by Paterson indicates that Paterson also tried progesterone in preeclamptic conditions and found that it improved the general condition and that the symptoms of intoxication diminished without a special diet. It was noted particularly that the albuminuria and the arterial tension decreased and that the edemas disappeared. After stating that Paterson made his studies with progesterone in twelve cases, van der Hoeven discusses two cases of pregnancy toxicosis in which he administered progesterone. Repeated tests on the blood pressure revealed that the progesterone effected only a temporary reduction, for, after a short time, the pressure increased again. The author further cites factors which indicate that progesterone is antagonistic to solution of posterior pituitary and that after treatment with progesterone the uterine muscle becomes less sensitive to

the effect of solution of posterior pituitary. Thus, in order to reestablish the sensitivity of the uterus to solution of posterior pituitary and facilitate normal delivery it is necessary to administer also estrogen. The author reports a case in which he resorted to the administration of progesterone and of estrogen. He reaches the conclusion that by treatment with progesterone and with estrogen it is possible to ameliorate provisionally all the severe symptoms of pregnancy toxicosis, after which it is necessary to provoke premature delivery in the usual manner.

## Presse Médicale, Paris

46: 1465-1480 (Oct. 5) 1938

\*Electro-Encephalographic Studies on Epileptic Patients. P. Pagniez, W. Liberson and A. Plichet.—p. 1465.

\*Action of Toad Venom on Heart. R. Lutembacher.—p. 1469.

Ureteropyelography in Nurslings. R. Bouchard.—p. 1472.

Angiocardiography in Children. A. Castellanos, R. Perciras and A. Garcia.—p. 1474.

**Electro-Encephalographic Studies in Epilepsy.**—Pagniez and his associates point out that the electrical activity of the normal and the diseased brain has been the object of many investigators during the last few years and that epilepsy has attracted the attention of electrophysiologists more than any other nervous disease. Their studies were made on thirty-three patients with diverse forms of epilepsy, in a small number of whom the diagnosis of epilepsy was doubtful. The electro-encephalograms were made with occipital, frontorolandic, biparietal, bitemporal and temporofrontal derivations (recording not simultaneous). In the course of these studies the authors observed paroxysmal as well as permanent modifications in the electro-encephalogram. They discuss and illustrate some of these modifications. They found that the epileptic patients with violent or frequent attacks and those refractory to treatment or with mental changes showed between the attacks electrical waves of abnormal frequency. In the majority of these cases the dominating frequency was between six and seven per second. Nevertheless, of twelve patients with the severe forms of epilepsy there were two who escaped to a certain extent this considerable retardation of the alpha waves, the predominating frequency being from eight to nine per second. Moreover, all the patients with severe epilepsy (except the patient who had been operated on) showed electro-encephalograms of great or average amplitudes (usually above 50 microvolts). The epileptic patients with less violent and less frequent attacks and those who were benefited by treatment did not show abnormal waves outside the epileptic attacks. Some of these patients, moreover, presented electro-encephalograms of small amplitude. Thus the electro-encephalograms of epileptic patients seem to be the objective indication of the severity of their disorder. This method of examination has not only diagnostic but also prognostic value. Moreover, it can be used for medicolegal purposes in the selection of persons for professions and for military service and in control of therapeutic measures.

**Action of Toad Venom on Heart.**—Lutembacher says that toads were widely used for the treatment of dropsy in patients with heart disease before digitalis was employed. After pointing out that the venom is excreted by the cutaneous glands and especially by the parotid glands of toads, the author reviews the earlier literature on the nature and action of toad venom. He first obtained and prepared the venom and then tested its action. He describes its effect on the heart action of various types of frogs and of rabbits and then describes clinical studies. The clinical observations confirmed the results of the experimental studies, that is they demonstrated that the action of toad venom is inferior to that of digitalis preparations in that it is of short duration. Finally the author demonstrates the immunity of the toad against its own venom. This immunity is related to the resistance of the toad to intoxication with digitalis.

46: 1481-1504 (Oct. 8) 1938

Kidneys and Arterial Hypertension. L. Langeron and R. Dehouck.—p. 1481.

\*Gold Treatment of Bronchial Asthma (Autodesensitization Under Influence of Thiosulfates). I. Vignati, V. Skalak and S. Ranchenberg.—p. 1482.

**Gold Treatment of Bronchial Asthma.**—Vignati and his associates describe clinical observations and animal experiments on the mode of action of the thiosulfates, particularly gold sodium thiosulfate, in anaphylactic conditions. Summarizing

their observations, they say that the antishock effects of the thiosulfates in bronchial asthma are due to the antianaphylactic effect of sulfur. The diverse cations intervene secondarily but they may appear preponderant by reinforcing or reducing the antishock effect of the thiosulfates and by modifying the metabolism of these substances. In the use of gold sodium thiosulfate it is necessary also to take into account the affinity of gold for the pulmonary tissue. In order to obtain a therapeutic effect, the presence of the allergen is necessary; the latter even plays the principal part by intervening at the moment when the thiosulfate effects a temporary desensitization. Its effect is thus produced according to Besredka's method; that is, by introducing intermittent doses into the organism. If the patient lives in surroundings rich in allergen, the desensitization renews itself incessantly and is so prolonged that it presents itself as a lasting disappearance of the sensitivity. It is this circumstance which is responsible for the lasting therapeutic effects. This justifies the assumption that the action mechanism is an auto-desensitization under the influence of the thiosulfates.

### Fisiologia e Medicina, Rome

9: 255-296 (July 20) 1938

\*Ascorbic Acid in Healing of Fractures. G. Giangrasso.—p. 255.

**Ascorbic Acid in Fractures.**—Giangrasso observed the healing of fractures in fifteen cases during the administration of subcutaneous injections of ascorbic acid after reduction of the fractures followed by immobilization or traction. The first injection of 0.005 Gm. of ascorbic acid was administered the same day the fracture was reduced. The following injections of 0.001 Gm. each were given at intervals of three days up to complete healing of the fracture, which was determined by the development of the fracture as shown by roentgenograms taken immediately before and after the local treatment and at weekly intervals in the course of the ascorbic acid treatment. Children received only half the dose given adults. The patients of another group who did not receive ascorbic acid but had the fractures treated in the same manner as the aforementioned patients served as controls. The author found that formation of a strong bone callus, restoration of the functions of the fractured structures and regaining of the working capacity took place in half the time in patients who received ascorbic acid as in those who did not. He believes, therefore, that ascorbic acid accelerates formation of bone callus in fractures and that the treatment is simple, economical and important socially and from the standpoint of insurance.

### Rivista di Chirurgia, Naples

4: 373-424 (Aug.) 1938. Partial Index

So-Called "Solitary Echinococcal Cysts" of Peritoneum: Case. P. Baiocchi.—p. 373.

\*Malformation of Pelvis and Predisposition to Inguinal Hernia. E. Rebusello.—p. 390.

Vaccine Therapy in Association with Chemotherapy with Azo Dyes in Acute Purulent Otitis Media. F. D'Onofrio.—p. 405.

**Malformation of Pelvis and Inguinal Hernia.**—Rebusello measured the length of the inguinal ligaments and the depth and width of the pelvis of eighty-seven men ranging in age from 20 to 68 who were suffering from inguinal hernia of various types. Hernia was bilateral in twenty-six of the cases. Simultaneous observations were made on a group of normal men of the same age as controls. Measures of the pelvis and of the inguinal ligaments were made after reduction of the hernia. The author found that the average length of the inguinal ligament in inguinal hernia is greater than normal (about 14 cm. or more, and 10.5 cm., respectively). Frequently the inguinal ligament is longer in the herniated than in the normal side in unilateral hernia and also longer on the side of the greater than on the side of the smaller hernia in cases of bilateral hernia. The upper transverse diameter of the pelvis is longer than normal (24.2 and 23.2 cm., respectively). The lower transverse diameter of the pelvis is normal or nearly so (30.2 cm.). The pelvis is of funnel-like shape. It is deeper than the normal structure (within 11.6 and 14.5 cm. in herniation, whereas in normal men it is 9.4 cm. deep). According to the author, the malformation of the pelvis predisposes to the development of hernia.

### Rivista di Clinica Pediatrica, Florence

36: 769-864 (Sept.) 1938

Volume of Blood in Normal Children. U. Gallerani.—p. 769.  
\*Blood Urea Clearance (Van Slyke) Test and Ambard's Constant in Children in Normal or Pathologic Condition. I. Biddau.—p. 805.  
Comparative Researches on Chemistry of Blood and Cerebrospinal Fluid in Poliomyelitis. S. Moschini and I. Biddau.—p. 834.

**Urea Clearance and Ambard's Constant in Children.**—Biddau observed the behavior of the Ambard constant and of the blood urea clearance (Van Slyke) in 110 children. The group included sixty-eight normal children and forty-two with renal diseases and diseases other than renal. The author found that the figures of Ambard's constant are the same for normal children as for normal adults (0.042 and 0.107 with an average of 0.07), the standard urea clearance (elimination of urine showing urinary secretion below the augmentation limit which is 1.7 cc. a minute) predominates over the maximal urea clearance (elimination of urine showing urinary secretion equal to or above 1.7 cc. a minute) and the figures of the urea clearance test are lower than in normal adults when the test is made during a period of functional rest of the kidney and almost the same when the test is made during functional activity. This is due to a special functional elasticity of the normal kidney, which is opposite to the functional rigidity of the kidney in pathologic conditions. The urea clearance and the Ambard constant agree in normal children. Low figures of the Ambard constant correspond to high figures of the blood urea clearance test. Both tests show normal renal functions in heart diseases. In lipoid nephrosis the results of the blood urea clearance show normal functions of the kidney whereas those of the Ambard constant show dysfunction (false results from influence of oliguria). In acute glomerulonephritis the figures of the clearance test are low and those of the Ambard constant are high in comparison to those of both tests in normal children. The author believes that the blood urea clearance test has the same applicability, diagnostic and prognostic value in children as it has in adults. The test is not changed by influence of extrarenal factors. It is more reliable than the simple determinations of urea in the blood and the results of Ambard's constant.

### Révista Argentina de Cardiología, Buenos Aires

5: 75-154 (May-June) 1938. Partial Index

\*Ventricular Complex in Electrocardiograms with Deviation of Electrical Axis to the Left. B. Moia.—p. 75.

Systolic Expansion at Level of Heart Ventricles. A. C. Morelli.—p. 97.  
Short PR Electrocardiographic Interval and Notched and Wide QRS Complex Showing Ventricular Asynchronism. B. Moia and L. II. Inchauspe.—p. 114.

Changes of Electrocardiogram in Parathyroprival Tetany. R. Dassen and R. G. Dambrosi.—p. 124.

**Ventricular Complex in Electrocardiograms.**—Moia studied 338 electrocardiograms with deviation of the electrical axis to the left (deep S wave in the third lead and R wave higher in the first lead than in the second lead) in a group of 316 patients. The QRS complex did not measure more than 0.1 second in any of the cases. During the last week the patients were not given digitalis before the electrocardiograms were taken. There were no pregnant women in the group. The electrocardiograms were classified in four different groups according to the behavior of the QRS complex in the third lead. The predominant features in the first group (224 electrocardiograms) were the existence of a short R<sub>3</sub> wave and a deep S<sub>3</sub> wave. The S wave was deep in the second lead in 122 electrocardiograms in the group. The second group (sixty-four electrocardiograms) showed a more or less deep S<sub>3</sub> preceded and followed by small positive R<sub>2</sub> and T<sub>2</sub> peaks (the triphasic complex). The third group (twenty-eight electrocardiograms) showed a deep Q<sub>3</sub> wave with or without changes of the R<sub>2</sub> wave. The fourth group (twenty-two electrocardiograms) showed the M or W ventricular complex. The electrocardiograms showed a normal heart in fifty-four cases in the whole group. The T<sub>2</sub> wave was negative in the electrocardiograms of normal hearts in all cases but three. It was positive in all cases of alterations of the heart. In the latter cases it was associated, as a rule, with a T<sub>1</sub> low or flat and with a deep S<sub>2</sub>. An inverted T wave was frequently seen in electrocardiograms of hearts either normal or slightly damaged. A downward deviation of the S-T

segment in the first and second leads with upward deviation of the segment in the third lead or an inversion of the T wave in the first and second leads showed alterations of the heart, especially enlargement and disturbances of the conductive system. The changes are not related to the type of the QRS complex in the third lead and do not appear in electrocardiograms of patients with slight myocardial alterations. A deviation of the S-T segment toward the largest ventricular deflection of the electrocardiogram or a negative T-S segment in the three leads shows myocardial alterations from disturbance of the coronary circulation. The associated presence of a deep  $S_2$  with a low  $R_2$  or of a small  $R_2$  with or without notchings and a more or less deep  $S_2$  show, in all cases, serious damage of the heart. The latter electrocardiographic changes, however, cannot be considered pathognomonic of either myocardial infarct or coronary lesion.

### Revista de la Asoc. Méd. Argentina, Buenos Aires

52: 827-894 (Aug. 30) 1938. Partial Index

Ménière's Disease. F. H. Quix.—p. 827.

Metastatic Epitheliomatous Nodules in Evolution of Cancer of Lung. N. Romano, R. A. Eyherabide and A. Danelli.—p. 831.

\*Ophthalmoscopic Sign for Intracranial Hypertension. J. Pereyra Kafer.—p. 835.

**Early Diagnosis of Intracranial Hypertension.**—The sign described by Pereyra Kafer is seen during ophthalmoscopic examination of the fundus of the eye. It consists in the diminution or absence of changes of the retinal venous circulation which are caused by bilateral compression of the jugular veins in the neck of normal persons. The changes consist in an increase of the caliber and darkening of the color of the retinal veins and diminution of the venous pulsation up to complete stopping, as compression advances and the energetic venous pulsation suddenly returns following sudden decompression (negative sign). The retinal circulatory changes do not take place in the presence of intracranial hypertension (positive sign). The author makes the ophthalmologic examinations with an ophthalmoscope for direct vision on the patient seated. An assistant, who stands behind the patient, performs bilateral compression of the jugular veins and subsequent sudden decompression in the course of the examination. The author obtained a negative response in 100 normal persons and a positive one in many cases of intracranial hypertension, fifteen of which are reported. He says that the diminution or lack of response in intracranial hypertension depends on the presence of hypertension of the retinal veins which develops earlier than edema of the optic disk. The sign is positive in intracranial hypertension of any origin. It appears earlier than edema of the disk and is reliable. When intracranial hypertension subsides, the sign changes from positive to negative.

### Archiv für klinische Chirurgie, Berlin

193: 1-753 (Sept. 21) 1938. Partial Index

Recognition of Hereditary Nature of Malformations. O. F. von Verschuer.—p. 185.

Etiology of Congenital Hip Dislocation. Rohleder.—p. 218.

\*Newer Concepts of Acute Pancreatic Necrosis and Its Treatment. O. Nordmann.—p. 370.

\*Treatment of Hemorrhage Due to Esophageal Varices by Ligation of Subdiaphragmatic Venous Anastomoses. C. Henschen.—p. 383.

\*Operative Treatment of Bronchiectasis and Pulmonary Tuberculosis. F. Sauerbruch.—p. 456.

**Acute Pancreatic Necrosis and Its Treatment.**—The process in the so-called acute hemorrhagic pancreatitis, according to Nordmann, is one of autodigestion and not of inflammation. He therefore prefers the name acute pancreatic necrosis. He believes that functional disturbances of the nerves of the blood vessels have a more important part in the causation of the disease than purely mechanical factors. These disturbances lead to the impairment of nutrition of the pancreatic cells, to formation of abnormal albuminous products and to activation of trypsin. Circulatory disturbances and fermentative processes are responsible for the autodigestion of the gland. The activation of trypsin results in the formation of products of high toxicity. At present there are no means of removing or of inhibiting these products either surgically or medically. The first phase in the anatomic alterations in acute pancreatic necrosis is edema not of an inflammatory but of an ischemic nature,

with beginning necrosis of cells. A number of intermediary stages lead to the conversion of the entire organ into one hemorrhagic, necrotic mass. Occasionally the process may be limited to a part of the organ. The author found diastase values increased in acute pancreatic necrosis. He feels, however, that the test is not of decisive value since it may be present in gallstone disease, in renal stones and in rickets. The increase in diastase is found during the first twenty-four or thirty-six hours, after which it rapidly falls. There may be a rise in the blood sugar level because of the destruction of insulin by activated trypsin. High blood sugar always suggests a bad prognosis. The diagnosis of acute pancreatic necrosis becomes suggestive in the presence of a history of gallstone disease, obesity, onset after a heavy meal, initial shock and vomiting of blood. The author points out that there is no point in draining the peritoneal exudate, since the latter is sterile, and while it contains trypsin it does not contain steapsin, which is injurious to tissues. Koerte advised the opening of the lesser cavity, drainage and tamponade in order to protect the rest of the peritoneal cavity. Next, the surgeons resorted to incision of the pancreatic capsule, and Nordmann advised, in addition, the removal of the gallbladder and inspection and drainage of the common bile duct. None of these measures, however, improved his results. The operative mortality has vacillated between 50 and 86 per cent. Nordmann had the experience of finding at operation a circumscribed area of edema in the pancreas, which prompted him to make a favorable prognosis, only to find at the postmortem a total necrosis of the organ. He concluded that operative manipulation of the pancreas aggravated the case. For that reason he and other surgeons have come to the conclusion that the fate of the patient with acute pancreatic necrosis is predetermined from the beginning and cannot be influenced by operative intervention. The author's mortality on the conservative regimen fell from 50 per cent to 24 per cent, Walzel's from 86 per cent to 28 per cent and Haber's from 53.6 per cent to 23.1 per cent. It is apparent that only about one fourth of the patients die if left alone. In cases in which the diagnosis is not certain, the author advises a simple exploratory incision. In the presence of acute pancreatic necrosis nothing should be done and the abdomen should be closed without drainage. In the presence of acute inflammation of the gallbladder with the patient not in a grave shock, Nordmann would remove the gallbladder and inspect and drain, if necessary, the common bile duct, but the pancreas is left alone. Secondary abscesses which may develop in the course of the conservative treatment are treated by incision and drainage. The most dangerous complications are hemorrhage from a large artery and pancreatic fistula. The prophylaxis of recurrence consists in operative treatment of the gallstone disease. The danger of subsequent diabetes is remote, but one should observe in these patients the blood sugar level.

### Treatment of Hemorrhage Due to Esophageal Varices.

—The possibility of surgical intervention in hemorrhages due to rupture of an esophageal varix depends, according to Henschen, primarily on the establishment of a correct diagnosis. The general examination may reveal the existence of a liver or a splenic disease of a type predisposing to the formation of varices, while the history may bring out one or more hemorrhages in the past, recent difficulty in deglutition, and cramplike pains of the esophagus radiating to the back or the sides. Aspiration of the esophagus with a soft thick stomach tube, after the drinking of water, may reveal blood clots. Other means are direct esophagoscopy and roentgenography. The medical treatment consists of a diet, morphine-atropine, introduction of a stomach tube, transfusions of small amounts of blood, tamponade either direct with the aid of esophagoscopy or through a gastrostomy opening, or direct compression with a colpeurynter. The operative measures include the use of the thermocautery, electrocoagulation with the aid of the esophagoscope, or cauterization through a gastrostomy opening (Lund and Foley). Hans Eppinger advised a splenectomy for recurring hemorrhage. This operation, in Henschen's opinion, is indicated in bleeding leukopenic-thrombopenic types of the splenic disease and is contraindicated in high grade polycythemia and in the presence of portal vein thrombosis. The elimination of the splenic venous flow, however, is not sufficient to prevent

a fatal hemorrhage from other tributaries of the coronary gastric vein. The logical procedure in Henschen's opinion is to ligate all the venous channels arising in the portal area and entering into the formation of the periesophageal and intra-esophageal varicose plexuses. This is best accomplished by a low intercostal thoracotomy on the left side extended by an incision in the diaphragm into a transdiaphragmatic laparotomy. Splenectomy may be performed at the same time if indicated by the presence of a leukopenic-thrombopenic state or when ligation of the splenic branches running to the esophagus is technically too difficult. In cases in which the removal of the spleen is hazardous (adhesions in thrombophlebitic splenomegaly) the author advises a partial ligation of the blood supply of the organ in order to bring about an oligemia rather than ischemia of the organ. He ligates the splenic artery and leaves the vein alone so that it may function in removing the products of breaking down of the organ. The author warns that operative intervention in patients with esophageal varices, whether due to liver cirrhosis or to another cause, is fraught with many dangers, such as the conversion of a small effusion into a permanent and extensive ascites or a dry cirrhosis passing into the ascitic phase. These patients are particularly predisposed to infection. Wound infection or postoperative pneumonia accelerates the progression of the cirrhotic disease. A compensated liver cirrhosis may become decompensated. The alcoholic patient is exposed to the danger of postoperative delirium tremens. Other complications are hepatic coma and cholemic bleeding.

**Surgery for Bronchiectasis and Pulmonary Tuberculosis.**—According to Sauerbruch, bronchiectasis develops as a sequence to inflammatory disease of the pulmonary tissue or as a result of trauma. Bronchiectasis in children and in the young was believed to be the result of pneumonia complicating scarlet fever, measles or pleurisy. The congenital dilatation of the bronchial tree as a forerunner of the condition here was not recognized until recently. In operating on young patients the author frequently found the bronchiectatic disease limited to one lobe. The finding of a dilated bronchus with hypertrophied or callous walls amid normal pulmonary tissue pointed to the congenital nature of the bronchial dilatation. Careful microscopic studies confirmed the gross observation. Congenital dilatation of a bronchus per se is innocent. It becomes pathologic only when, as a result of a superimposed inflammation, the secretions cannot be coughed up from the dilated sacs. This leads to continued suppuration and the development of bronchiectatic disease. Mechanical narrowing of the thoracic cavity by rib resection or filling could be effective in bronchiectasis of inflammatory etiology. Bronchiectasis of congenital origin demands more radical therapy, namely the removal of the involved lobe. The operative treatment of pulmonary tuberculosis is based on the concept that the latter is a general constitutional disease. The paravertebral thoracoplasty with resection of the first to the tenth or the eleventh rib was developed as the result of careful anatomic studies. In his own clinic the operation had a mortality of 2.3 per cent and a cure in from 60 to 80 per cent when the disease was limited to one side. In less carefully selected cases the proportion of cures amounted to from 40 to 42 plus 30 per cent of the cases which showed improvement. In 1,600 cases in which there were broader indications for operative intervention the mortality was 6 per cent and the cures 40 per cent. The operation of filling, first conceived by Tuffier as pneumolysis and later developed by Baer as a paraffin filling, is useful in the treatment of hollow spaces in cured tuberculosis and again as an aid in unsuccessful thoracoplasties. The method was found to be particularly valuable in the treatment of productive cirrhotic process of the upper lobe with small but stiff-walled cavities. It may be applied in severe acute hemorrhage, and it made possible the operative treatment of bilateral involvement. In the treatment of cavities it is important to recognize two types, the early cavities with elastic circumference and the rigid cavity of tertiary phthisis. The author sees much advance in partial thoracoplasties limited to the seat of the disease. Among the important recent concepts he emphasizes that of Ranke, who called attention to the dependence of anatomic tissue reactions on allergy and the immune-biologic status of the body.

## Archiv für Ohren-, Nasen- und Kehlkopf., Berlin

145: 97-236 (Sept. 13) 1938. Partial Index

- Question of So-Called "Dental" Empyema of Maxillary Sinus. K. Amersbach.—p. 97.  
Etiology, Types and Terminology of Tonsillogenic Sepsis. A. Linck.—p. 103.  
Dangers of Local Anesthesia in Tonsillectomy: Their Causes and Prevention. A. Linck.—p. 131.  
Simplified and Harmless Anesthesia in Tonsillectomy. J. Schubel.—p. 138.  
Spontaneous Hemorrhages of Palatine Tonsils. A. Linck.—p. 143.  
\*Acute Otitis Media and Nephritis. W. Giese.—p. 159.

**Acute Otitis Media and Nephritis.**—Giese studied twenty-seven cases of nephritis in patients with acute otitis media, which were observed at the otolaryngologic clinic of the University of Jena during the years from 1932 to 1937. These twenty-seven cases of simultaneous nephritis and acute otitis media represent 2.45 per cent of the 1,103 cases of acute otitis media which were treated during that period. Among the 403 cases of chronic otitis media, nephritis was never observed. The twenty-seven cases of concurrent nephritis and acute otitis media are classified into four groups, which differ greatly as regards type and course of the disease. In the first group of seven cases an acute nephritis developed in addition to an acute otitis media. The nephritis developed either several days or several weeks after the onset of the otitis media, usually following after a new attack of general infection, which was recognizable on the increase in temperature. Generally the nephritis is independent of otitis media, but it may originate in the ear as the result of a surgical trauma by way of the blood stream. In the second group of two cases an acute nephritis became complicated by an acute otitis media. These cases were characterized by a severe disturbance in the general condition. The otitis media developed independently of the nephritis but, as a result of the inadequacy of the defense powers of the organism, the otitis media developed sooner than would be the case otherwise. In the third group, which comprised sixteen cases, acute otitis media and acute nephritis developed simultaneously, frequently accompanied by diseases of other organs, particularly the rhinopharyngeal organs. The general condition is extremely poor. It cannot be determined from the outset and the course of the disease whether the nephritis is dependent on the otitis media. In the fourth group of two cases an acute otitis media developed in addition to a chronic nephritis. Observations revealed that the aural and renal diseases concurred and did not influence each other noticeably. Thus a real dependence of the nephritis on the otitis media cannot be detected in all cases and the author rejects the notion that acute otitis media is a focal infection. The concurrence of acute otitis media and nephritis as well as of other local diseases is the result of a general infection which is frequently of tonsillogenic or pharyngogenic origin. The concurrence of oral and renal disease makes no essential difference in the therapy. Surgical treatment is not necessarily more urgent or more frequent. Treatment of the ear exerts little influence on the severity or the course of the nephritis. The ear and the kidney should be treated in the usual manner and a thorough general therapy should be combined with the treatment of these organs.

## Zeitschrift für klinische Medizin, Berlin

134: 671-818 (Sept. 15) 1938. Partial Index

- Esophageal Electrocardiogram. O. Spühler.—p. 671.  
Morbus Cushing in Patient with Ovarian Teratoma. E. Krönke and G. W. Parade.—p. 698.  
Einthoven's Triangular Diagram as Foundation of New Electrocardiographic Methods of Registration. H. E. Hollmann and W. Hollmann.—p. 732.  
\*Sugar Content of Cerebrospinal Fluid and Its Relation to Blood Sugar in Healthy Persons and in Patients. A. von Bothmer.—p. 754.  
Influenza and Weather. J. Bauer.—p. 778.

**Sugar in Cerebrospinal Fluid and Blood Sugar.**—Von Bothmer mentions the diurnal alimentary and emotional fluctuations of the blood sugar and calls attention to the fact that the fluctuations in the sugar content of the cerebrospinal fluid occur later and are weaker than those of the blood. Then he discusses the factors which influence the exchange between blood and the cerebrospinal fluid. In the second part of his



paper he takes up the relation between the sugar content of the cerebrospinal fluid and that of the blood under normal conditions and in the third part he discusses this relationship in the course of diseases. The normal range of the sugar content of the cerebrospinal fluid and the normal ratio between the sugar content of the cerebrospinal fluid and that of the blood was determined on 105 healthy persons. To determine the conditions in pathologic processes, 378 examinations were made simultaneously on the cerebrospinal fluid and the blood of patients with various diseases. In his studies on normal persons the author found that, as the sugar content of the blood increases, the sugar content of the cerebrospinal fluid also shows a tendency to increase; that is, it is impossible to talk of a normal range of the sugar content of the cerebrospinal fluid which is independent of the blood sugar. However, the ratio between the sugar content of the cerebrospinal fluid and that of the blood is not constant. It is higher in the cases with low blood sugar values than in the cases with high blood sugar values. The author's observations on the ratio between the sugar contents of cerebrospinal fluid and blood differ from those of some other investigators. His opinion of the sliding adjustment of the normal ranges suggests that the active secretory function of the ependyma of the plexus has a tendency to aim at a "normal" height for the sugar content of the cerebrospinal fluid. This secretory function is strong when the blood sugar is low, weak when the blood sugar is high. However, the secretory activity is counteracted by physicochemical forces, which apparently are responsible for the fact that even in case of increased blood sugar content the ratio between the sugar contents of the cerebrospinal fluid and of the blood does not fall below a certain absolute value. The author's studies in pathologic conditions revealed that the determination of the ratio is of greater diagnostic significance than is the determination of the absolute sugar content of the cerebrospinal fluid. Reductions in the ratio occur in tuberculous meningitis, purulent meningitis, influenzal meningitis and syphilitic meningitis. Increases in the ratio are not specific for certain diseases and consequently are of slight value for the differential diagnosis; their diagnostic value lies in the fact that they usually indicate a diffuse and severe cerebral lesion.

### Hospitalstidende, Copenhagen

81: 889-916 (Sept. 13) 1938

\*So-Called Traumatic Thrombosis in Axillary-Subclavian Vein. E. Roelsen.—p. 889.

Biologic Establishment of Vitamin C in Woman's Milk. P. W. Bræstrup and H. Lieck.—p. 913.

**Traumatic Thrombosis in Axillary-Subclavian Vein.**—Roelsen says that in this disorder there is an acute venous stasis, in part recurrent, manifested by marked venous dilatation and diffuse swelling of the upper extremity. The pathogenesis is uncertain. The syndrome is usually due to preceding overexertion or movement of the arm causing strain, also presumably to certain predisposing anatomic variations in the conditions about the course of the axillary-subclavian vein over the first rib. The mechanism is believed to vary somewhat in different cases. Thrombus formation must be considered a complication, most often due to certain predisposing changes in the wall of the vein or to more or less latent infections; it is not the main cause. The syndrome as a rule occurs in younger, healthy persons without preceding disturbance, particularly in men, and especially on the right side. The general condition is usually not affected. On complication with thrombosis there is often a slight rise in temperature. Complete restitution is the rule, but the time required varies from weeks to months and years, depending partly on the treatment. As long as the venous stasis or the tendency to recurrence persists, the condition invalidates manual laborers up to one third of the normal ability. The author advises first the trial of conservative treatment. Venolysis and denudation of the wall of the vein can be attempted in resistant cases. As a last resort venesection can be tried. The theoretical basis for the operation is not yet clear. Seven personal cases are reported, of which three were treated operatively.

### Ugeskrift for Læger, Copenhagen

100: 1015-1044 (Sept. 8) 1938

Casuistics from Surgery of Jaw. J. Foged.—p. 1015.

\*Treatment of Patients with Acute Suppurative Otitis Media, with Special Regard to Value of Syringing with Alcohol. V. Schmidt.—p. 1018.

\*Treatment of Patients with Acute Suppurative Otitis Media by Syringing with Alcohol. A. Jørgensen.—p. 1022.

Röntgen Treatment of Chronic Medical Disorders of Joints. S. Heimd.—p. 1027.

Spiritism as Causative Factor in Psychic Disturbances. H. Reistrup.—p. 1031.

**Alcohol for Otitis Media.**—Schmidt says that in acute inflammation of the middle ear treated by his method the functional results, without after-treatment with the air douche, have been particularly good, the number of operations small, the mortality low and the average hospitalization not longer than with other conservative treatment. Early paracentesis is called for, after which hot compresses are applied for twenty-four hours. Syringing with 33 per cent by volume or 27 per cent by weight of alcohol at 37 C. is then begun. A record syringe of from 10 to 20 cc. is used, with a rubber disk attached to the cone and held to the external ear. The fluid reaches the tympanum under a certain pressure by which the discharge on the tympanum is more readily removed with the fluid as it flows back to the disk. Individualization is necessary as to the frequency and number of treatments. In rare cases irrigation three or four times a day suffices, six times daily is the rule, and more frequent daily flushings are given in cases of high temperature and a tendency of the paracentesis opening to close. Paracentesis was repeated in less than every tenth patient. The patients often notice alcohol in the rhinopharynx, which shows that the eustachian tube has become passable, favorably increasing the drainage of the middle ear, with simultaneous rapid improvement in hearing. Syringing with 27 per cent alcohol causes pain only when the treatment is delayed, so that the canal is raw. If there is pain from the mucous membrane of the middle ear, a 2 per cent solution of nupercaine is added for the first days. The author asserts that as far as he knows the combination of disinfection and astringent action with improved drainage of the middle ear through syringing with alcohol is not attained by any other agent. Of the 103 patients treated in 1936 twelve, or 11.7 per cent, were operated on; of these eight had mastoiditis on admission. After-examination in 1937 of 218 patients, most of whom had been observed for more than a year, showed that neither mastoiditis nor other complications had followed. In 210 cases the tympanum had healed, in twenty-five with small cicatrices, mostly linear; in five cases there were small, sharp-edged perforations, with normal hearing, in one a larger central perforation, in two a moist inner ear. Hearing was normal in 208 cases. In the complete material of 295 cases from the period of treatment with syringing with alcohol the mortality was about 1 per cent; two of the three patients who died were operated on immediately after admission.

**Treatment of Otitis Media with Alcohol.**—In the course of a year all of Jørgensen's patients with otitis media were, if immediate operation was not indicated, treated by syringing with alcohol according to the Schmidt method, either twenty-four hours after paracentesis in recent otitis or from the day of admission in cases of spontaneous perforation or paracentesis done before admission. There were 357 patients, with 509 cases of acute suppurative otitis media. In three cases treatment had to be terminated because of unbearable pain in connection with the syringing, in most cases there was pain from two to five minutes after irrigation, especially during the first days, and a few patients felt no pain. In 247 cases recovery resulted; in about two thirds of these the treatment was begun twenty-four hours after the incision of the eardrum, in one third at a later stage. Seventy-five patients, or 29.3 per cent, were operated on in spite of the treatment. The 410 patients with 584 cases of acute suppurative otitis media from the preceding year constitute the control material. Of these 37.8 per cent were operated on. The author sees as drawbacks the need of hospitalization, the painfulness of the treatment and the long duration of the treatment; the advantages are the reduced number of patients operated on, the infrequency of a second paracentesis, the absence of eczema in the middle ear and external ear, and the possibility for direct effect on the middle ear and the eustachian tube.

# THE STUDENT SECTION

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## Medicine and Civil Government

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NEW YORK

No longer ago than 1910 the students of the University of Edinburgh were congratulated by Sir William Osler on the unexcelled thoroughness with which the prevention of the acute infective fevers had been carried out in Scotland and the fact that the death rate of their city was among the lowest in Europe (15.3 per thousand). And yet if our New York Metropolitan Area should now suffer from such high rates as then and there prevailed, great would be the medical and social consternation, hysterical the publicity, and high the probability of a change of city government.

If a drop in the death rate from 15 to 10 per thousand of the population could express so considerable an alteration of professional and public attitude and such a different perspective in social conscience and ambition, what may have been some of the enduring and effective factors? Among these we like to think that society has become more sensitive to human suffering and that government has responded to social influences.

As Dr. Osler said, "The human heart by which we live has been touched as with the wand of a Prospero. What availed the sceptered race! What the glory that was Greece, or the grandeur that was Rome! Of what avail even has been the message of the gospel, while the people at large were haunted by fear and anxiety, stricken by the pestilence of the darkness, and the sickness of the noonday?"

So, the much beloved master of modern medicine saw the picture but little before you, our students of today, were born.

Now with the intervening record of war and confusion, both ethical and material, we cannot say as he did that "The outlook for the world as represented by Mary and John, and Jennie and Tom, has never been so hopeful." It is for us here and now to challenge as he did then "the dour dyspeptics in mind and morals who sit idly croaking like ravens—let them come into the arena, let them wrestle for their flesh and blood against the principalities and powers,

represented by bad air and worse houses, by drink and disease, by needless pain, and by the loss annually to the state of thousands of valuable lives—let them fight for the day when a man's life shall be more precious than gold. Now alas! the cheapness of life is every day's tragedy."

### THE PUBLIC HEALTH

The social change of outlook grew in strength with the spreading net of knowledge of the quantity and causes of preventable sickness and death. This took practical form in nations, states and cities within a score of years in the middle of the last century, by the action of voters and legislators who determined to include within civil government those functions devoted to protection of the general health of the population, so far as this could be achieved by the application of public authority, the employment of appropriate personnel and the expenditure of tax money. This marriage of the medical sciences to government has, it would seem, been among the highest achievements of mankind in his ever increasing social ambition to master the safety of his body and soul as well as to build a security for his goods. As one moves about in spirit or in fact among the nations the suspicion is strengthened that, of the three gospels, that of man's body is on the whole better served than are those of his spirit or his material wealth, and yet the concern of government with men's bodies has been of more recent origin than its interest in their credos or its control over their tangible property.

While various ancient civilizations have left material records of their intelligence in matters of cleanliness for the person, the home and the city, and in spite of the hygienic regulation of individual and social conduct by religions and dynasties of distant times, the permanent continuous use of the knowledge of human biology within the structure of civil government is a matter of such recent origin as to be almost contemporary with the present most productive era of the medical sciences.

Even the classic treatise of Johann Peter Frank in 1777-1778, when he completed the

Opening address before the Columbia University College of Physicians and Surgeons, Sept. 28, 1938.

publication in Mannheim of his "System einer vollständigen medicinischen Polizei," was too far ahead of his times to have any tangible effect on the forms or functions of the government of the Palatinate or the kingdom of Bavaria.

It was the "Gesundheits Catechismus" of Bernard Christoph Faust that for some forty years after its publication in 1785 became a part of the elementary school education in Würzburg, Darmstadt, Cassell, Hanover and Hamburg. But this did not involve any substantial innovation in government or initiate new functions, merely expanding and formalizing a part of the school curriculum and clarifying the essential elements of the teaching of hygiene. It was not until 1848 when the parliament of Great Britain wrote its first public health law that there was incorporated in this form and duty of public service that element which has so amazingly influenced human life around the world.

#### BASIC FEDERAL STATUTES

While the germ of our own federal public health service, first so named officially in 1912, appeared in the obligation of the Treasury Department in 1789 to provide for the medical care of merchant seamen, it was not until 1893 that the Congress enacted those basic federal statutes on which the inclusive and ever broadening duties with which we are now familiar are based.

The first state department of health was established in Massachusetts in 1855 and the first metropolitan board of health with powers sufficient for all emergencies and essential functions was created by act of the legislature of New York in 1865.

It is with proper medical humility that we recall that it was the lawyer, actuary and secretary of the Poor Law Commissioners of England, Edwin Chadwick, who provided the survey of 1838, stimulated public response and developed support for the first national health law, and another lawyer and student of vital statistics, Lemuel Shattuck, who made the commonwealth of Massachusetts conscious of her health hazards and with his survey of 1854 brought the need of the public to the legislators' attention. Again it was the lawyer Dorman B. Eaton of this city who drafted the law of 1865 under which the Metropolitan Board of Health of New York operated and did it so well that it has been the model of many successors across the continent. The facts about life and death in this city, and the principles on which a modern municipal department of health was created, developed out of the famous sanitary survey conducted largely by the voluntary services of teachers and graduates of our College of Physicians and Surgeons.

It has been notable that parallel with the constantly expanding functions, best or only to be served by government for protection of the

public health, there has been a rapid broadening of those of the private physician in both teaching and applying for the individual and family the precepts and procedures on which the best results of governmental activities in the last analysis inevitably depend.

It is notable that those forms of government most broadly based on the participation of men and women in the conduct of their own local and national civic affairs have been most responsive to the demand of the public for a constantly expanding use of the most recent discoveries of the biologic and medical sciences through government.

Authoritarian government seems to have lacked something essential in its application of science for human betterment. The records of the best national health are where the student, the teacher, the private and public practitioner of human biology, the doctor of medicine, are least hampered by administrative restrictions and the health officer of government is closely responsive to the informed social and professional opinion of his community.

#### GOVERNMENT AND MEDICINE

Many and varied have been the definitions of the objectives sought by the combined sources of government and medicine in the interest of health, from exuberant all-inclusive utopian expressions to the more modest goal of the professional worker. It was Sir George Newman, the distinguished former chief medical officer of the British Ministry of Health, who, as guest of the Academy of Medicine of this city, expressed briefly his most ambitious hopes for the function of the sciences and arts of preventive medicine, "To build a better tabernacle for the soul of man to inhabit," truly a high ideal for a profession or a state.

In its simplest terms public health consists in the application of the sciences of preventive medicine through government for social ends, and it is with this that we are concerned. At the moment sound distinctions between the functions of government and those of the independent and the responsible private practitioner of medicine are in some danger of being swept away in a wave of immature emotional, if not actually political, governmental dominance, implemented by the power of redistribution of the amount and objects of public expenditure for health and other medical services, and are threatened with extinction by the ponderance of federal opinion and tax resources.

There is perhaps still time, though barely enough, to bring to the present problems of medicine and government that slow careful study and trial which has served social evolution so well in the past.

It should be noted that while almost a century of experience with official services,

demanding and gladly accepted by the public and maintained by taxes for reducing the hazards of life by the application of preventive medicine, has made clear the distinction between what each of us can, should and must do ourselves, individually, to promote our health, and what can be done for us only by government, or at least at less cost through public service, there is neither the experience nor any substantial evidence to justify the belief that the entry of government extensively into the practice of curative medicine would achieve results comparable in the scientific, social or economic sense with those attained in public health.

Medicine, whether curative or preventive, has more to contribute than it has ever been able to deliver in the past, and by wise organization certain still greater benefits may be assured; but to reason from the productive success of preventive medicine through government for social ends that diagnosis and treatment of the individual medical and surgical patient by or under the professional and financial control of government would similarly advance social ends or the quality of medical care, or reduce its cost, is not only questionable but on its recorded performance elsewhere is at least improbable.

#### OUR PRESENT HEALTH STATUS

It is well to pause a moment before forming a fixed opinion or committing ourselves irrevocably to a repetition of the blunders and complexities which have arrested the progress of medicine in some other lands and consider the eminence of our own present health status. Certainly no 130,000,000 people under one government or federation of states, and no aggregation of populations representative of such different races or distributed so widely under varied conditions of climate, occupation and economic status have in the recorded history of man enjoyed such relative certainty as our people of the United States do today in the survival of their offspring in infancy and childhood, or have experienced so low an incidence of the communicable diseases or so high an average level of life expectancy. And yet in the most recent official declaration from technical committees and interdepartmental boards in Washington we read that "preventive health services for the nation as a whole are grossly insufficient."

In spite of the fact that no other such continental population has built and served hospitals so lavishly, it is true that some backward and impoverished states and particularly scattered rural populations have not yet been reached by institutional care for general illness, which is now within an hour's motor ride of more than 98 per cent of our people. These same unfavored areas lack also almost all the other conveniences and safeguards, amenities

and cultural advantages of more fortunate regions of the nation. Perhaps time, patience and ingenuity in thrift are needed more than any such vast expansion of hospitals as is proposed by the federal government.

While the honest medical Diogenes searches, and generally in vain, to find persons really needing and wanting but not receiving medical attention, those who use the flood lights of unlimited publicity rather than the discriminating lantern of knowledge suddenly wring our hearts and amaze our international neighbors with the statement that "one third of the population, including persons with or without income, is receiving inadequate or no medical service." It has been estimated that about one third of our population patronizes the charlatan, the quack and the practitioners of therapeutic cults. Perhaps it is this fraction of our people that is referred to by the spokesmen of the federal government, though their words imply failure of the organized profession of medicine.

How can we add to a proper humility, as disciples of Aesculapius, acknowledgment that the abracadabra of legislation and the pompous self sufficiency of bureaucrats can and will do for one in three of our people what we as physicians have failed to do in response to the call of the sick for help?

May we not for a moment play the role of economists or sociologists and answer the fourth item of indictment with which the so-called National Health Program is launched?

"An even larger fraction [i. e., more than one third] of the population suffers from economic burdens created by illness."

Is it possible that economic confusion has been created by international fear and distrust, by class hatred encouraged by the very government that should serve all classes, by a long accumulating disproportion between the capacity of industry to produce and of the wage earner to consume, and that much illness is the sequel of economic burdens rather than chiefly their cause?

#### SUCCESS IN LIFE SAVING

It could probably be statistically demonstrated that preventive medicine has saved from diseases and deaths which afflicted our grandparents' generation in this country about as many persons now living as constitute the great army of the unemployed and unemployables. Our very success in life saving has certainly been a factor in creating a surplus in the labor market.

The phenomena we are facing in the relations of medicine to government, to society, to economics, to federal taxation and federal subsidies for purely local needs are too unfamiliar to the public, to the medical profession and to the Congress to permit us to accept as if final or con-

clusive the evidence offered by a technical quintet, none disciplined by or experienced in the responsibilities of independent medical practice, or by a sextet of appointed executives whose attitude cannot fail to be responsive to the expediencies of their own and their chief's political careers.

It has been said that "untroubled certainty and assured consistency" may be vouchsafed only to those who are not wholeheartedly committed to the scientific attitude of mind in the solution of their problems.

It is well known that government is a large participant in the dual system of institutional care of the sick, almost to the exclusion of private care in the management of hospitals for tuberculosis, mental diseases and those of acute communicable character, and for general illness among persons unable, at least when sick, to pay for medical attendance and hospital care. The safety and chief merit of any hospital service is the tradition and effective practice of medical staff control of policies and standards of professional care of the patients. The medical board and the clinical pathologic conference are instruments of superior value in preventing laxity in medical and surgical performance, whatever may be the limitations imposed by administration.

The same delicately adjusted balance of reciprocal functions of the government and the individual physician as exists in the main in the field of public health will have to be recognized, accepted and stabilized by law and practice in the general care of the sick before we shall have a sense of freedom from threat of government destruction of the individual practitioner of medicine, on whose broadly conceived functions the best in modern life depends.

#### OFFICIAL HEALTH AGENCIES

Whether in the simplest form of township, county or little city organization for health, or in great states, nations or in the Society of Nations, there are but half a dozen functions of government carried on by the work of official health agencies, which have everywhere been found necessary, to supplement the efforts and resources of the individual practitioner in relation to the families he serves. Within the definition of organized care of the sick there are as many as eight fields of service now occupied by governmental and voluntary agencies, and in each of these the control over quality of care of the sick properly rests with the professional staff responsible for the diagnosis and treatment.

Specious arguments are commonly offered, based on the fact that we have common services of police, fire, public conservancy of streets, water and sewage, and that we accept public schools for the compulsory education of

our children, to persuade us that similarly tax-supported and officially administered services for sickness should be conducted by government, wholly or in part at the taxpayers' expense.

While the assistance of government may be useful, although not essential, in facilitating thrifty practices of the family in providing by periodic prepayment for the calculable incidence and necessary costs of disease, there is no reason in the experience of other countries now or in the past to justify us in creating a compulsory contributory system of support for medical care in which the physician and the patient no longer enjoy free choice of economic and professional relationship.

We can afford to take the problem piecemeal, test new devices of governmental participation, measure results in terms well tried in experience, and avail ourselves of the forty-eight experimental fields of civil government which our states offer, before plunging headlong into some national program, ill adapted to the infinite variety of our needs and resources, under the pressure of political expediency and visionary hopes.

Representative government and medicine have been partners in well doing too long to have their initial concern interrupted by temporary differences of opinion or judgment. A doughty individualist, a colleague in physiology from a sister university, has recently taken the opportunity of a tribute to the late S. Weir Mitchell to make the query "Is it not true that, when men have bartered their personal freedom for collective security, they have lost freedom without gaining a security worth having? Is it not a fact that cave fishes have some security—but no vision, while the eagle has scant security but enjoys both vision and wings?"

#### RELATIONSHIP OF TEACHER AND PUPIL

And so we start another season of that academic association so dear to scholars, and your teachers indulge in the perennial renewal of their confidence in human nature through their privilege of converse with you, their fellow students, separated only by the accident of age. Let me, on behalf of your teachers, express my acknowledgment of our debt to you and your successors, by contact with whom alone we continue to play our part in this collegium, of which I am reasonably sure you will grow to be inordinately fond.

Bear in mind the experience of our own particular medical philosopher, Sir Thomas Browne, who in introducing himself to his reading public said:

Now for my life, it is a miracle of thirty years, which to relate were not a History but a piece of Poetry, and would sound to common ears like a Fable. For the World I count it not an Inn but an Hospital,

and a place not to live in but to dye in! The world that I regard is myself, it is the microcosm of my own frame that I cast mine eye on.

Surely Sir Thomas Browne would have rejoiced to hear the words of a modern manufacturer of motor cars who warned the students of a Michigan college of the hazards of today: "Your battle is against the most insidious and tireless of foes . . . the wishful thought, the tempting short cut, the shallow assumption, the clever expedient, the evasion of responsibility, . . . and the specious solution, . . . the surrender of independence and integrity of mind."

Permit me in closing to relate a personal episode from which my earliest interests in medicine and government developed:

In September 1895, when I began the daily walk from my home at Twenty-Eighth Street and Madison Avenue to our college on West Fifty-Ninth Street, I spent many an evening and all free week-ends until Election Day soliciting

votes for the anti-Tammany ticket, as election district captain in the old and notorious "Tenderloin" district, under the direction of the district leader, now the president of our university. This was my initiation to the concern of our profession with public affairs.

You, the students of today, walk the brief space from Bard Hall or the subways and take for granted the general honesty and increasing competence of our city government. You see at last included in our educational community a municipal health center, the material symbol of a participation of government in applied medicine.

I beg of you, the elder workers in this sanctuary, to be patient with the clatter and dirt, the noise and shadows of the new home of the youngest specialty of the medical sciences, the Institute of Public Health, and its collaborator in the training for the governmental services of medicine, the city of New York.

## Comments and Reviews

### STUDENT JOHN SHAW BILLINGS

The experiences of medical students sometimes contribute to the development of powerful ideas. A notable example was an experience of student John Shaw Billings, the centennial of whose birth was celebrated this year. Billings was born in southeastern Indiana and was graduated from Ohio Medical College in Cincinnati in 1860, after earning his way by residing in the hospital and later taking care of the dissecting rooms of the college. In writing his graduating thesis on the results of surgical operations for the treatment of epilepsy, he found it was practically impossible to review the literature. In order to find the data in their original form, he consulted many books and ransacked libraries in Cincinnati, Philadelphia and New York. After six months of such harrowing work and correspondence, he learned there was then not a medical library in the United States in which a student could find a large part of the literature on any medical subject. It was necessary for investigators to visit the capitals of Europe to be reasonably sure of having seen all the reports made by previous investigators on a given subject. It was this experience, Billings said some thirty years later, that caused him to try to establish for American physicians a complete medical library and an index of medical literature which would spare investigators the impossible task of consulting thousands of texts to find a few references. Thus was born the idea from which developed the greatest medical library in the world today, the Army Medical Library in Washington, D. C.

After graduating, Billings began to practice in Cincinnati; but in a short time the Civil War came along and he entered the Medical Department of the United States Army, serving at the battles of Gettysburg and Chancellorsville, in field hospitals, and in hospitals in New York harbor. In 1864 he was detailed to the Surgeon General's Office in Washington, and here his genius found an opportunity to develop. The Surgeon General's Library at that time comprised 2,253 volumes. A fund of about \$80,000, left over from the Civil War hospital funds, was entrusted to Billings in 1868 to use for the improvement of the library, and at once he embarked on the great work that eventually was to make it possible and practical to review the medical literature. He began collecting and cataloguing and in 1872 published the first Catalogue of the Surgeon General's Library, which comprised 454 pages with a supplement of twenty-six pages. Two years later he published a three volume catalogue. His vision, however, was much broader. He wanted a catalogue in which under the names both of authors and of subjects the literature of the world would be indexed. He prepared a specimen and submitted it to leading members of the profession throughout the country in 1876. When their approval was received, he began to prepare the famous Index Catalogue of the Surgeon General's Library, which, Edgar Erskine Hume<sup>1</sup> says, marked an epoch in the development of medical literature. Physicians who formerly

1. Hume, Edgar Erskine: *The Centennial of the World's Largest Medical Library: The Army Medical Library of Washington, Founded 1836*, M.H. Surgeon 78:241 (April) 1936.



obtained data and reviews in a haphazard way now have the literature of the world indexed in a convenient form. The first series of the Index Catalogue, comprising sixteen volumes, was published between 1880 and 1895; the second series, of twenty-one volumes, between 1896 and 1916, and the third series, of ten volumes, between 1918 and 1932. The first three volumes of the fourth series have more recently been published. The Index Catalogue is the most comprehensive bibliography ever attempted in any field. Its preparation, Sir William Osler said, is gargantuan. Dr. William H. Welch said that it is the greatest contribution of America to medicine.

John Shaw Billings had other talents. As Garrison shows in his memoir,<sup>2</sup> Billings designed the great Johns Hopkins Hospital in Baltimore. He was in charge of vital statistics during the tenth and eleventh census of the United States and was in part responsible for the development of the United States Public Health Service. He became professor of hygiene in the University of Pennsylvania; he consolidated and catalogued the three public libraries of New York City. He was the author of numerous publications, among which were<sup>3</sup> "A Sanitary Survey of the United States," "The Cholera Epidemic of 1873 in the United States," "Reports and Papers on the Johns Hopkins Hospital," "Reports on Barracks and Hospitals," "Reports on Diseases of Cattle in the United States," and his classic "Literature and Institutions." His greatest achievement, however, was the development of the Surgeon General's Library and the Index Catalogue. The development of student Billings into the great librarian makes it possible even today for physicians in any part of the United States to have access to much of the medical literature of the world, for on request through their local library they can borrow for a short time books and periodicals from the Army Medical Library in Washington, D. C.

### HOW TO REVIEW MEDICAL LITERATURE

The librarian of the New York Academy of Medicine, Dr. Archibald Malloch,<sup>1</sup> recently addressed the Hartford Medical Society at a dinner in honor of Dr. Walter R. Steiner, who for thirty-five years has been librarian of the society. Dr. Malloch said that physicians should be insured against certain risks which they may encounter after graduation: the risk of being satisfied with methods of diagnosis and treatment learned in medical schools; the risk of being content with what is good instead of

striving for what is better; the risk of intellectual or mental laziness which often comes to those in the midst of a busy practice; the risk of becoming rusty. The kinds of insurance against these dangers which the speaker suggested were: (1) the study of disease in private patients as well as in hospital practice and the recording of this experience in carefully taken notes; (2) discussion of problems at meetings of medical societies; (3) the publishing of brief papers about your cases; (4) the perusal of medical journals and books, so that it becomes a habit. "To study the phenomena of disease without books is to sail an uncharted sea, while to study books without patients is not to go to sea at all." These were the words of William Osler.

It is good for a physician to purchase a system of surgery and read some part of it every day; and, likewise, for a surgeon to read a system of medicine, making notes as he reads. The reading habit stimulated Bigelow to say that Oliver Wendell Holmes could get what he wanted out of a book as dexterously as a squirrel can take the kernel of a nut out of the shell.

Medical literature is indexed so well that work in the libraries is easier than if one were studying almost any other profession. The speaker did not refer to the very old bibliographies but mentioned first the *Index Medicus*, which was published in three series between 1879 and 1926, except that from 1900 to 1902 its place was taken by the *Parisian Bibliographica Medica*. In 1927 the *Index Medicus* joined with the *Quarterly Cumulative Index*, which had been published by the American Medical Association since 1916. The combined indexes were then published under the title *Quarterly Cumulative Index Medicus*, which continues to be published by the American Medical Association. You may readily see, Dr. Malloch said, that to find the articles and books which have been published on a subject, you would have to look in all the volumes of the *Index Medicus* and in all of the semiannual volumes of the *Quarterly Cumulative Index Medicus*. The great John Shaw Billings, the centennial of whose birth has been celebrated this year, was the father of the *Index Medicus*. He planned and brought out also a much more comprehensive work, the *Index Catalogue of the Surgeon General's Library*, which is still being published. The *Index Catalogue* began in 1880 and had passed through three series of volumes by 1932. The first volume of the fourth series appeared in 1936 and the second volume in 1937; the other volumes in the fourth series will appear from time to time. Each volume of the *Index Catalogue* covers all the medical literature in the Army Medical Library that is indexed under one or more letters of the alphabet, at the time of going to press. The *Index Catalogue* is an

2. Garrison, Fielding H.: John Shaw Billings: A Memoir, New York, G. P. Putnam's Sons, 1915.

3. Kiser, Edgar F.: John Shaw Billings of the Centenary of the Army Medical Library, J. Indiana M. A. 29:424 (Sept.) 1936.

1. Malloch, Archibald: A Short Talk on Medical Libraries, J. Connecticut M. Soc. 2:223 (May) 1938.

author and subject index in one alphabet, the books, reprints and theses appearing under "author," while under "subject" are found the books, theses and titles of all magazine articles. In the first series of the *Index Catalogue* was indexed all the old and new books in the Army Medical Library at the time, as well as all articles printed in old journals on down from the time of their beginnings. What a piece of work!

The second series of the *Index Catalogue* indexed the old or ancient books which had come to the library after the first series was published, and also old journal articles. The fourth series indexes under an author's name the old editions of his books that have been obtained since the corresponding volume of the third series was issued. Each volume of the *Index Catalogue* includes now about twenty years of modern literature. In attempting to find what has been written, for instance on the subject of pneumonia since the beginning of time, one has only to look at the volumes in the first, second and third series of the *Index Catalogue*, which list the publications on pneumonia, instead of looking at the many, many volumes of the *Index Medicus*. One should bear in mind, however, in connection with the third series of the *Index Catalogue* that in the volume Ge-Izzet Bey and later volumes no journal articles published after the end of 1925 were included. Articles not included in the third series will, however, be included in the volumes of the fourth series covering Ge to the end of the alphabet. For more recent articles on subjects not dealt with in the first two volumes of the fourth series of the *Index Catalogue*, one must consult the volumes of the *Quarterly Cumulative Index Medicus*.

Thus if one is writing a paper, the way to review the literature is to look at all titles of books and articles on one's subject listed in the volumes of the different series of the *Index Catalogue* and then go through all the volumes of the *Quarterly Cumulative Index Medicus*. What a historical perspective this will give! Do not let anyone look over these lists for you, Dr. Malloch advised, or you will miss much of great value. The greatest physicians that he has known have written their own papers, including the preparatory work. As you go through the lists, he continued, select the titles of monographs or articles that you wish to read. Look also at systems of medicine or surgery, for the titles of their articles are not given systematically in the published indexes. Should your library not possess all these books or journals, ask to borrow them from the Army Medical Library. Keep notes on little points that you desire to look up in the library. Visit the library regularly to see the new books and journals as they come in, and read what you wish of them. Browsing in libraries is a source

of great pleasure and profit. It was Osler's habit to go to the library of the Medical and Chirurgical Faculty of Maryland in Baltimore several times a week before dinner, and to make notes of what he read.

### THE SOCIAL SIDE OF MEDICAL PROGRESS

*Abridgement of an address before the annual meeting of the Minnesota State Medical Association, Duluth, June 30, 1938, by Dr. Howard W. Haggard of Yale University Medical School, New Haven, Conn., and published in Minnesota Medicine, October 1938.*

It is well at times to draw back a little from the details of immediate and practical projects and in contemplation to view medical and social situations in broad perspective, to see trends, directions and dimensions.

Viewed in this way the feature that shows as peculiar to the present period is the rapid shift and change of long established social institutions. As we watch these changes, the realization is forced on us that the body of society is a delicately integrated entity so interdependent in its parts that a change in any one must necessarily result in a change in all other parts, in a total readjustment.

Thus if medical discovery is made and applied to the saving of lives, there must follow a reorganization of society as a whole. The saving of life results in a change in the age structure of the population. The change in the age structure of the population upsets the balance of the established institutions and necessitates social and economic readjustments.

It is axiomatic in our field that, as one disease diminishes, others rise to take its place. As the incidence of tuberculosis, typhoid, dysentery and smallpox go down, cancer and diseases of the circulatory system rise correspondingly. The change in the leading causes of death in the last thirty-eight years is common-place knowledge.

Sometimes I think the physician fails to see that medicine itself is one of the institutions affected by the changes that are brought about. Medicine does not stand alone; it is an integral part of society. In the face of such change there appears one of the peculiarities of medicine: the failure to realize that it must change as society changes. The medicine of today may be vastly different from the medicine of the past but the fact remains that the social and sociological forces that guide it operate on it today just as they did in the past.

The great danger that I see to the practice of medicine today lies in the very thing that has given medicine its modern preeminence, and that is science. The physician has committed himself to science. He stands or falls with it. My indictment tonight is against this science—

a science that has led the doctor to neglect the equally fundamental and nonscientific social aspects of medical practice—those things that we sometimes sum up as the art of medicine, a thing about which the younger generation of physicians knows so little. The doctor, in making a fetish of science, may find himself worshipping alone. He will unless his medical practices are changed continually to suit precisely the society in which he lives.

The doctor of America in the eighteenth and early nineteenth centuries was not a scientist. He was a public-spirited man whose medicine suited the times. He was a social leader, embodying the rare combination of medical practice and sociology. We today look with pity, mingled with contempt, on the practices of Benjamin Rush. Yet, in spite of his lack of science, Rush as practitioner and medical leader has no equal today. The tenet of the young physician today is too apt to be the reverse of that of Rush.

The reason for the mode of thought that pervades medicine today is not hard to find. In the last hundred years, with the introduction of the exact sciences into medicine, medical research has yielded some of the most beneficial knowledge that the human race has ever acquired. Enthusiasm has grown high and a mode of thought crystallized. The science of medicine has been elevated; the practice of medicine, which is not a science and never will be, has been subordinated.

The emphasis on research has resulted in the development of an aura of sanctity about research. The acquisition of knowledge has received and still receives a cultivated regard amounting almost to a veneration, and one out of all proportion to the regard given to the application of the results of research. This mode of thought, scientific research—the search for novelty, the new—is inculcated in the medical student and hence in the physician; it has given a direction to medicine. And the movement has developed an inertia so that medicine cannot readily turn to new directions, although those directions are clearly indicated.

Medical science is not medical practice. The great benefits from the application of preventive medicine that so dominate the public mind today are not those of medical practice. These matters are science and being science they do not require the participation of the practitioner. Any aspect of medicine that has been reduced to an exact science needs merely medical technicians and not physicians for its accomplishment. Such is the case with much of our diagnostic tests. At one time it required the consummate skill of the physician to determine in some cases the presence of syphilis; now a far more accurate diagnosis is made by a

technician in the laboratory. When—and if—medicine becomes an exact science we shall no longer need the practicing physician. Until it does become an exact science, then we not only need him but we should grant him his due and proper importance.

#### THE ART OF THE PHYSICIAN

The practicing physician is not a scientist. He is, if he really practices medicine, more, far more, than a scientist. He is an artist. He does not deal with the controlled and limited matters of the laboratory; he deals with human beings. So long as the human mind in its full ramifications remains beyond an evaluation with scientific precision, then the practice of medicine must remain an art. So long as medical practice involves the personal contact of physician and patient, then it is the art of the physician which must establish the necessary bond. This is very different from medical research. It is, in many ways, more difficult. It involves not only intelligence and skill but also qualities of personality unnecessary to the research worker.

In the first flush of the triumphs of the application of science to medicine, it appeared that all the problems of medicine were to be answered and that medicine at last was destined to become as exact and impersonal as engineering. In consequence, to the eventual great detriment of the practice of medicine, our medical education was changed. It adopted the precise methods of science. It built its structure on the laboratory as a foundation.

#### MEDICAL EDUCATION

Let us trace the broad steps in the change in American medical education. A century and a quarter ago French medicine went through one of the periodic changes of direction. The old formal dogmatic teaching gave way to an active clinical investigative type of medicine. Germany, following the Napoleonic wars, was in the throes of a wave of idealism and romanticism that denied in the medical schools factual investigation and permitted only speculation. It was one of the extremes of the pendulum movement of education. Then it swung the other way; by the middle of the century German preclinical medicine had been founded by Johannes Müller. His pupils, including Virchow, give the roster of the famous teachers and investigators of Germany. Almost without exception, and this includes Müller, they were men with enormous social interests. Virchow, you will remember, was as fearless and fiery in his political activities and his denouncements as he was in the classroom. The best of German medicine was gradually brought to America. The part that caught and held attention was the research aspect. At first the leading schools in this country were

famous for their clinical teachers. The pre-eminence of Johns Hopkins in the closing years of the last century and the early years of this century was based on its great clinicians. Today, with the continual swing of the pendulum toward research, the preeminence of a school is judged not by how well it trains doctors for the practice of medicine but on the eminence of its researches. The chairs once occupied by great clinicians with wide social interests and wide social influences are too often filled by scientists out of touch with the real problems of the practitioner. Few great scientists have been eminent physicians. Formerly students in our schools were trained to be socially beneficial. Now they are trained too often with the apparent intention of making laboratory investigators out of them and that in spite of the fact that medical practice is a social application. Too often today we train not physicians with all the significance of the term but, instead, bedside pathologists.

Medical training is being divorced from medical practice; preclinical training is being sold out to educators who are not even physicians. The emphasis on science, on the laboratory, has extended down even into the premedical field in the college. The selection there is made on the basis not of socially minded individuals who would make good practitioners but of aptness in the laboratory subjects. The class of men who enter Eastern colleges are today, as potential material for social leadership, distinctly inferior to the young men from the same colleges entering law and business. We are turning away good men because no matter how great their ability might be as practitioners they show no aptitude for the technic of medical research.

#### SOCIALLY MINDED PHYSICIANS

There is a greater need for socially minded public-guiding physicians than at any previous period in medicine. The diseases that come to the front in the modern medical readjustment cannot be cured or prevented by impersonal science. They can be controlled only by the close and intelligent cooperation of the individual members of the public with the physician. Obtaining this cooperation is a vastly different matter from acquiring the knowledge of how to prevent or treat the disease. It is not medical research or science; it is the practice of medicine in its broadest service of a social leadership.

The social worker today knows that the greatest, indeed probably the only possible field of social betterment is offered by medical application. Some aggressive lay groups stand ready to raid the medical field for its unapplied potentialities. With the natural reaction of newcomers to the field, they assume there is something basically wrong with the form of

medical practice. Their first inclination is to remake the form of medicine.

Public opinion determines the condition and future of medicine. Advancement, construction, is not made by great numbers but by great individuals. It isn't what medicine does, it isn't what science discovers, that gives the necessary high public regard to the physician. It is what the public thinks and believes. The physician, in casting his lot with scientific research, stands and falls with it. And he has chosen an uncertain support. A social disturbance destroys first of all medical science. A little over a hundred years ago there was no medical science in Germany. Then in half a century Germany raised herself to world pre-eminence in medical science. And then in the present century, under changing social conditions, medical science declined in Germany; it is disappearing; it has already gone in Russia, Italy and Spain. We still have it, but it remains at the mercy of social change.

The permanent basis of medicine is not its research, but its social application—its practice.

#### APPLICANTS FOR ADMISSION TO MEDICAL COLLEGES

The study of applicants for admission to the freshman class of 1937 at seventy-eight medical colleges in the United States, published in the *Journal of the Association of American Medical Colleges*, is the tenth study of this kind made by Dr. Fred C. Zapffe,<sup>1</sup> secretary of that association. These annual studies provide reliable data on the number of applicants for admission to medical colleges, the action taken by the colleges, and the basis of acceptance and rejection. The number of applications for admission to the medical schools has increased from 29,705 in 1933 to 35,439 in 1936. The number of applicants accepted, however, has steadily declined from 7,419 in 1934 to 6,410 in 1937. Nearly 11 per cent of accepted applicants in 1937 did not enroll.

The 1937 freshman class was the smallest in ten years. The agreement between the Council on Medical Education and Hospitals of the American Medical Association and the Association of American Medical Colleges that there should be one full-time teacher for each twenty-five students in the preclinical departments has tended to make smaller classes. When general business conditions are good, attendance in medical colleges falls off, and vice versa; the attendance reached a record high in 1932 and has since declined. From 23 to 25 per cent of students entering will not graduate. About 200 repeaters enter every freshman class, 75 per cent of whom fail to make good.

1. Abstract of a paper by Fred C. Zapffe, published in the *Journal of the Association of American Medical Colleges*, May 1938.

Women multiple applicants have increased at a greater rate than men; there were 60 per cent more women multiples in 1937 than in 1933. Otherwise the number of women applicants has followed the same trend as that of the men applicants. Sixty-two per cent of women applicants were accepted in 1933, 52.4 per cent in 1937 (52.5 per cent of men were accepted in the same year). The total of accepted women applicants remains under 400 each year.

The number of medical students who have had less than three years of college work is decreasing each year. Accepted applicants of this group constitute 9.2 per cent of all accepted applicants. Of all applicants, 32.6 per cent have had three years or more of college (no degree) and 54.7 per cent of this group were accepted. The degree group represented 52.1 per cent of all applicants; 55 per cent of this group were accepted. Applicants are not discriminated against on the basis of college work taken, if the scholastic record is good.

Data are submitted on the total number of applications made in 1937 to seventy-eight

medical schools. Five schools (Columbia, Northwestern, Pennsylvania, St. Louis and Temple) had more than 1,000 applications each. The maximum was 1,263 (Pennsylvania). These schools and twelve others enrolled more than 100 students each. Nine schools (including six two-year schools) had less than 100 applications. Thirty of the schools enrolled less than sixty students each.

In 1937, data on 5,643 multiple applicants show how they fared as to acceptance. The group has increased 22 per cent since 1933 but acceptance of multiples has declined 11 per cent in five years. Single applicants have diminished 10 per cent in five years. Thirty-two per cent of multiples made two applications, about 40 per cent made from three to five applications, about 18 per cent from six to ten applications, about 8 per cent from ten to twenty applications and the remainder more than twenty applications. Many multiples continue to make applications for years with no acceptances; one person made seventy applications in three years.

## Medical College News

*Medical schools, hospitals and individuals will confer a favor by sending to these headquarters original contributions, reviews and news items to be considered for publication in the Student Section.*

### Stanford Students Active in November Election

The student body of Stanford University School of Medicine, San Francisco, took an active part in the November 8 election with regard to State Proposition No. 2 on the ballot, which was said to be misnamed the "Humane Pound Act." The student body said "it is a vicious threat to the health and well-being of the public, camouflaging regulations of animal pounds." It proposed to prohibit the use of animals by universities, medical schools and laboratories for scientific purposes. The proponents of this bill, the student body said, "show an utter disregard for the invaluable knowledge with which biologic research has equipped the physician to battle disease." As future physicians charged with the responsibility of the maintenance of health and the prevention and cure of disease, the student body urged the defeat of the so-called Humane Pound Act. The California voters defeated the proposal.

### Larger Quarters for Interns

Two additional floors on the Administration Building of the University Hospital, Ann Arbor, Mich., are to be constructed to provide for the housing of the entire intern staff within the main hospital building. In addition to sleeping quarters there will be recreation rooms and lounges for the interns and hospital staff. The two houses which now are occupied by some of the interns will be released for other purposes.

### American Student Health Association

The annual meeting of the American Student Health Association will be held December 29-30 at the Hotel New Yorker, New York City.

### Fellowships in Anesthesiology

Graduate fellowships in anesthesiology have been established by the Medical School and Graduate School of the University of Minnesota, Minneapolis, for physicians who desire to prepare themselves for the practice of this specialty. The fellowships offer an abundance of clinical training in all types of local, regional and general anesthesia and gas therapy, and also adequate related graduate work in chemistry, anatomy, physiology and pharmacology. Applicants must have served at least one year in a rotating internship.

### Iowa Promotions

Dr. Ewen M. MacEwen, dean, State University of Iowa College of Medicine, Iowa City, announces the following promotions on the faculty:

Harry M. Hines, Ph.D., associate professor to professor of physiology.

Waid W. Tuttle, Ph.D., associate professor to professor of physiology.

Dr. William F. Mengert, assistant professor to associate professor of obstetrics and gynecology.

Dr. John H. Randall, assistant professor to associate professor of obstetrics and gynecology.

Dr. Emory D. Warner, assistant professor to associate professor of pathology.

Dr. Thomas L. Waring to assistant professor of orthopedic surgery.

Dr. James A. Greene, assistant professor to associate professor of theory and practice of medicine.

### Michigan Personals

Marshall L. Snyder, Ph.D., teaching assistant in bacteriology at the University of Michigan Medical School, Ann Arbor, has been appointed instructor in bacteriology. Vivian G. Behrmann, M.S., assistant in physiology at the University of Michigan Medical School, has resigned to accept an appointment in the Woman's Medical College of Pennsylvania, Philadelphia.

### New Teachers at University of Tennessee

The following appointments to the faculty of the University of Tennessee Medical School, Memphis, have been announced:

Dr. Kendall B. Corbin, formerly of Stanford University, Calif., to be associate professor of anatomy.

Frank Harrison, M.S., formerly of Northwestern University School of Medicine, Chicago; instructor in anatomy.

Howard C. Peters, Ph.D., formerly of the University of Minnesota Medical School, Minneapolis; instructor in physiology.

Dr. Robert A. Bussabarger, formerly of Detroit; instructor in pharmacology.

Charles C. Rainey, Ph.D., formerly of Berry College, Mount Berry, Ga.; instructor in chemistry.

### Four Year Course in Preventive Medicine

A grant of \$84,000 from the Commonwealth Fund has been made possible at New York University College of Medicine, New York, for a new program on preventive medicine which will comprise studies covering a four year period. In the announcement the dean, Dr. Currier McEwen, is reported to have said that the nucleus of the new department of preventive medicine was the Hermann M. Biggs professorship in preventive medicine, established years ago as a memorial to the late Dr. Biggs, who was a pioneer in public health work. The expansion of the department at this time is in recognition of the work of the late Dr. John Wyckoff. Dr. Harry Stoll Mustard will be director of the department and the program will be conducted by a full time staff of instructors and technicians. Instead of concentrating studies in preventive medicine in the last two years of regular medical college work, it will now begin in the freshman year. A teaching and research center will be provided in the facilities of the lower East Side Health District, the use of which has been made possible through the cooperation of the New York City department of health.

### Maryland Personal

Dr. Charles D. Smith has resigned as chief resident of the Radiological Department of Johns Hopkins University School of Medicine, Baltimore, and has entered private practice at Richmond, Va.

### Wayne University News

A total of \$45,000 has been accepted by the Wayne University College of Medicine, Detroit, in support of research and teaching at the college of medicine. The largest single gift was \$10,000 for the establishment of a research laboratory in ophthalmology. Dr. Parker Heath, professor of ophthalmology, has charge of the laboratory. Gordon L. Walls, Sc.D., has been appointed research associate in ophthalmology.

### Texas Personals

Drs. Isaac P. Barrett and Harold M. Williams, Fort Worth, assistant city health director and city epidemiologist, respectively, have been awarded scholarships for public health studies at Vanderbilt University, Nashville, Tenn.

### Three Generations of Doctors

With the graduation of Drs. James B. Witherington and Albert S. Witherington, Millington, in September from the University of Tennessee School of Medicine, Memphis, there have been three successive generations of physicians in the Witherington family. Dr. Albert S. Witherington Sr., Millington, graduated from the Memphis Hospital Medical College in 1904 and his father, Dr. James B. Witherington, Munford, from Vanderbilt University School of Medicine, Nashville, in 1878.

### Six Surgeon Generals from University of Pennsylvania

The University of Pennsylvania School of Medicine, Philadelphia, is credited in the October *Pennsylvania Gazette* with having graduated six surgeon generals of the United States Army Medical Corps. They were Clement A. Finley, who graduated in 1818 and served as surgeon general from May 15, 1861, to April 14, 1862; Joseph K. Barnes, who graduated in 1838 and served as surgeon general from Aug. 22, 1864, to June 30, 1882; Robert Murray, who graduated in 1843 and served as surgeon general from Nov. 23, 1883, to Aug. 6, 1886; William H. Forwood, who graduated in 1861 and served as surgeon general from June 8, 1902, to Sept. 7, 1902; Robert M. O'Reilly, who graduated in 1866 and served as surgeon general from Sept. 7, 1902, to Jan. 14, 1909, and the present surgeon general, Charles R. Reynolds, who graduated from the University of Pennsylvania in 1899 and was appointed surgeon general in 1935, after many years of distinguished army service.

### Faculty Changes at Columbia

The following medical appointments and advancements at Columbia University, New York, have been announced:

Associate Professor, Dr. Milton Carl Peterson (New York Post-Graduate Medical School).

Assistant Professors: Dr. Virginia Apgar, anesthesia; Dr. Gaston Arthur Carlucci, clinical surgery; Dr. Beatrice Maher Kesten, clinical dermatology; Dr. Rafael Rodriguez-Molina, tropical medicine (School of Tropical Medicine); Dr. Jose Rodriguez Pastor, bacteriology and hygiene (School of Tropical Medicine); Dr. Otto Klineberg, psychology; Clarence R. Carpenter, Ph.D., anatomy.

Assistant Clinical Professors: Drs. Abbott William Allen, medicine (New York Post-Graduate Medical School); Zacharias Berco-vitz, medicine (New York Post-Graduate Medical School); John Dorsey Craig, pediatrics (New York Post-Graduate Medical School); John Staige Davis Jr., medicine (New York Post-Graduate Medical School); Frank Miller Falconer, medicine; Julian Maxwell Freston, medicine; Samuel Waldron Lambert Jr., medicine; Robert McGrath, medicine (New York Post-Graduate Medical School); Thomas Turlay Mackie, medicine; Theodore Neustaedter, gynecology (New York Post-Graduate Medical School); Robert Louis Preston, orthopedic surgery (New York Post-Graduate Medical School); Theodore Campbell Thompson, orthopedic surgery.

### New York Personal

Dr. Ralph E. Knutti, assistant professor of pathology at the University of Rochester School of Medicine, New York, addressed the students and faculty of the West Virginia University School of Medicine, Morgantown, September 23, on "Plasma Protein Regeneration."

### Appointments at Duke University

The following appointments were made recently to the faculty of the Duke University School of Medicine, Durham, N. C.: Dr. Harold W. Brown, professor of preventive medicine and public health; Dr. James P. Hendrix, associate in medicine, and Hans Neurath, associate in biochemistry.

### South Carolina Personal

Dr. S. C. Werch, demonstrator in physiology at the School of Physic, Trinity College, Dublin, has been appointed instructor in the department of pharmacology in the Medical College of the State of South Carolina.

### Fordham Opens New Pharmacology Laboratory

Fordham University, New York, has opened a newly equipped laboratory for applied physiology and pharmacology in the Pharmacy Building on the campus, in conjunction with the inauguration of a new course leading to the degree of Bachelor of Science in Pharmacy. The laboratory will be used



for the new courses in physiology and pharmacology for the sophomore and junior students in B.S. courses in pharmacy and for graduate students who wish to further their studies. It is fully equipped for research, and apparatus for the study of body function and drug action is available for student use. The laboratory will be under the direction of Leonard J. Piccoli, Ph.D., professor of materia medica, pharmacology and physiology. Its facilities will also be used by the seniors and graduate students of biochemistry who are taking courses in anatomy and physiology under Dr. Piccoli.

#### Wisconsin Personal

Malcolm R. Irwin, Ph.D., associate professor of genetics, University of Wisconsin, Madison, addressed the university medical society October 27 on "The Inheritance of Resistance to Bacterial Infection."

#### Changes at the University of Texas

The board of regents has approved the following appointments to the faculty of the medical branch of the University of Texas, Galveston:

Dr. John L. Otto to the department of neurology, replacing Dr. Martin L. Towler, resigned.

Dr. James H. Herrod to the department of obstetrics, replacing Dr. Charles M. Mulherin, resigned.

Drs. Elva A. Wright, Fred B. Smith, Frank J. Hams and Adair W. White, staff members of Jefferson Davis Hospital, Houston, who will serve without pay in the department of obstetrics.

Dr. Wylie F. Creel to the practice of medicine department, replacing Dr. Michael B. Shimkin, resigned.

Dr. Robert A. Edwards as graduate assistant in the practice of medicine.

Dr. Charles E. Webb assistant in surgery, Dr. Clyde E. Thomas Jr. junior assistant in surgery, and C. C. Scott assistant in physiology.

#### Tennessee Personal

Cleveland S. Simkins, Ph.D., associate professor of anatomy, University of Tennessee College of Medicine, Memphis, has resigned to become head of the department of anatomy at Creighton University School of Medicine, Omaha, effective September 15. After receiving the degree of doctor of philosophy at Harvard University in 1921, Dr. Simkins was appointed assistant professor of histology at the University of Tennessee. He was appointed associate professor of anatomy in 1923.

#### Iowa Personal

Dr. Raymond G. E. Bunge, of Imlay City, Mich., has been appointed to the staff of the department of urology, University Hospital, at the University of Iowa, Iowa City. Dr. Bunge interned two years at the University Hospital at Ann Arbor, Mich., after receiving his M.D. in 1936 from the University of Michigan.

#### New Pathology Building at Georgia

The construction of a new laboratory and classroom building to house the departments of pathology and bacteriology at the University of Georgia School of Medicine, Augusta, was begun September 28. The new building will be adjacent to the Dugas Building, which also is new, and the cost of construction will be \$70,000.

#### District of Columbia Personal

Dr. Walter Andrew Bloedorn, professor of medicine in the School of Medicine of the George Washington University, Washington, D. C., and medical director of the University Hospital, has been appointed acting dean of the school of medicine.

#### Michigan Awards the Sternberg Medal

The Sternberg Memorial Medal, which was established in honor of the late Dr. George M. Sternberg, formerly surgeon general of the United States Army, is awarded annually to the medical student who has made the best record in preventive medicine. The award is made by the faculty on the recommendation of a committee. The winner in 1938 was Dr. William Kaufman.

#### Kentucky Personals

Dr. Jackson M. Thomas has resigned his position as associate professor of psychiatry at the University of Louisville School of Medicine to enter the department of psychiatry at Harvard University, Boston. Dr. William K. Keller has been appointed to fill the vacancy. Dr. Keller, a native of Louisville, recently completed a year of study in London on a Rockefeller fellowship.

#### Scholarships and Fellowships at Harvard

Harvard University Medical School, Boston, has awarded sixty-three scholarships totaling \$25,578 to medical students and has also awarded twenty-four fellowships totaling \$21,650 for the coming academic year. The names of the fellowships together with the recipients and the departments in which they work are given in the following list:

Edward Austin Fund Teaching Fellowships: Oliver H. Lowry, biochemistry; Duncan E. Reid, obstetrics; Bernard R. Hodes, physiology; James M. Parker, surgery.

Edward Hickling Bradford Fellowship for research: Francis S. Cheever, bacteriology.

John White Browne Scholarship for research: Smith Owen Dexter Jr., medicine.

William Story Bullard Fellowships for research: Arnold Max Seligman, chemistry; Bernard David Davis, physical chemistry; Lawrence C. Kingsland Jr., medicine.

Arthur Tracy Cabot Fellowship for advancement of surgery: John E. Dunphy, surgery.

James Jackson Cabot Fellowship "to aid and encourage practical work in scientific medicine": John Holmes Dingle, surgery.

DeLamar Student Research Fund: Bernard German, bacteriology; Nathan B. Kurnick, physiology; Stanley M. Levenson, public health; Edward Meilman, biochemistry; John Holmes Dingle, surgery.

Louis E. Kirstein Fellowship: Louis H. Nason, surgery.

William O. Moseley Jr. traveling fellowship for study in Europe: Dale Gilbert Friend, biochemistry; Rolf Lium, surgery; John Burton Dynes, psychiatry.

Francis Weld Peabody Memorial Fellowship for intensive clinical and laboratory studies: Arnold P. Meiklejohn, medicine.

Jeffrey Richardson Fellowship for continuation of studies either here or abroad: Lewis Dexter, medicine.

The Whitman Fund, for pursuing the study of medicine or surgery at the Ecole de médecine de Paris: John Burton Dynes, psychiatry.

Dr. William Hunter Workman Scholarship to enable graduates of Harvard Medical School to pursue postgraduate studies in medicine in this country or abroad: Robert P. Tucker, biochemistry.

#### North Dakota Personal

Dr. Russell A. Nelson, Minot, N. D., a graduate of Johns Hopkins University School of Medicine in 1937, has been appointed assistant resident physician at Johns Hopkins Hospital, Baltimore, and assistant instructor in medicine at Johns Hopkins University.

#### The Holden Trust Fund at Western Reserve University

Western Reserve University, Cleveland, came into possession of the principal of the Albert Fairchild Holden Trust Fund August 25, which was the twenty-fifth anniversary of the death of Liberty E. Holden, who established the foundation as a memorial to his son. The fund, which is said to be worth at least a million and a half dollars, will continue to be used, as directed by Mr. Holden, for lectures and research in the School of Medicine.

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## THE MEDICAL MANAGEMENT OF CHRONIC ULCERATIVE COLITIS

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Chronic ulcerative colitis remains one of the most controversial problems in the field of disorders of the gastrointestinal tract. Opinion is divided with respect to classification. There is marked divergence of opinion concerning the natural history of the disease and its prognosis. There is no agreement concerning etiology, and no uniformity in the various philosophies of treatment.

It is apparent from the literature that the criteria for classification must be altered. There has been and still is a school of thought which regards the associated bacterial flora as the fundamental index rather than the anatomic and physiologic changes which the disease produces. Thus, by the operation of such a system of nomenclature, the isolation of *Shigella dysenteriae* in a case presenting chronic inflammatory lesions of the colon automatically excludes the case from the group styled chronic ulcerative colitis. Such arbitrary subdivision is made without respect to the pathology, physiology or natural history of the disease. Two evils result: There is constant pressure to restrict rather than to broaden the scope of investigation. The inevitable confusion of thought leaves the clinician hopelessly lost in a sea of argument at cross purposes.

Morbid anatomy constitutes the proper basis for classification. The fundamental pathologic condition of chronic ulcerative colitis may be defined as the sum of necrosis plus productive inflammation. This creates the varied pictures seen under the microscope and in gross specimens. There is diffuse destruction of normal tissues, inflammation accompanied by hemorrhage and intense polymorphonuclear infiltration, fibroblastic proliferation and later formation of dense and extensive collagenous scar tissue. Recognition of these changes automatically excludes from consideration conditions such as amebiasis, tuberculosis and syphilis, which present characteristic and distinctive pathologic pictures.

Differing hypotheses have been advanced to account for the development and progression of these lesions. The concept of infection is widely held. A variety of micro-organisms have been proposed as the primary agents.

Hurst<sup>1</sup> has long considered the disease to be the result of continued infection by *Shigella dysenteriae*. The proponents of this hypothesis base their views largely on the results of the agglutination reaction. Dysentery agglutinins, however, are frequently present in the absence of demonstrable homologous infection.<sup>2</sup> Furthermore, there is evidence to indicate that these antibodies appear in response to heterologous infection by certain strains of *Escherichia coli*.<sup>3</sup> Dysentery bacilli have been isolated in approximately 20 per cent of the cases that I have seen in New York City.<sup>4</sup>

Bargen<sup>5</sup> and his associates hold that a specific diplococcus is responsible and that this organism can be recovered in 80 per cent of the cases.<sup>6</sup> The specificity of this organism has been denied. Strains obtained from the Mayo Clinic have been shown to differ among themselves in their behavior in culture and in heat resistance. Their serologic characteristics are not uniform and there is close immunologic relationship with strains of *Enterococcus*.<sup>7</sup> Other investigators have failed to recover the diplococci in a large proportion of their cases.<sup>8</sup>

More recently an anaerobic bacterium has been advanced as the primary agent.<sup>9</sup> In like fashion most of the bacteria recoverable from the human colon have, at one time or another, been suggested as important etiologic factors.

Andresen<sup>10</sup> first reported that food allergy plays a definite role in certain cases of chronic ulcerative colitis. The clinical evidence on which this conclusion was based is supported by experimental data. Allergy is characterized by sensitization and immunity, which may develop separately. Sensitization followed by exposure to the specific antigen produces allergic inflammation which may be accompanied by actual necrosis of tissue. Inflammation is known to favor local fixation of anti-

1. Hurst, A. F.: Ulcerative Colitis, *Guy's Hosp. Rep.* **71**:26-41 (Jan.) 1921.

2. Mackie, T. T.: The Specificity of the Agglutinin Reaction for *Shigella Dysenteriae*: I. The Agglutination Reaction in Chronic Bacillary Dysentery: A Serologic and Bacteriologic Study of Forty-Seven Cases, *Arch. Int. Med.* **62**:783 (Nov.) 1938.

3. Mackie, T. T.: The Specificity of the Agglutinin Reaction for *Shigella Dysenteriae*: Agglutinin Absorption Relationship Between *Shigella Dysenteriae* and *Escherichia Coli*, to be published.

4. Mackie, T. T.: Ulcerative Colitis: I. The Relationship Between Bacillary Dysentery and Ulcerative Colitis, *South. M. J.* **27**:492-499 (June) 1934.

5. Bargen, J. A.: Experimental Studies on the Etiology of Chronic Ulcerative Colitis: Preliminary Report, *J. A. M. A.* **83**:332-336 (Aug. 2) 1924.

6. Buie, L. A.: Practical Proctology, Philadelphia, W. B. Saunders Company, 1938.

7. Totrey, J. C., and Monton, E.: Comparative Observations on Streptococci from Human Gastrointestinal Ulcerations and from Bovine Mastitis, *J. Infect. Dis.* **58**:105-114 (Jan.-Feb.) 1936.

8. Rafsky, H. A., and Manheims, P. J.: The Significance of the Bargen Organism as an Etiological Factor in Ulcerative Colitis, *Am. J. M. Sc.* **183**:252-256 (Feb.) 1930.

9. Dack, G. M.; Dragstedt, L. R., and Heinz, T. E.: Bacterium Necrophorum in Chronic Ulcerative Colitis, *J. A. M. A.* **106**:7-10 (Jan. 4) 1936.

10. Andresen, A. F. R.: Gastrointestinal Manifestations of Food Allergy, *M. J. & Rec.* **122**:271-275 (Sept. 2) 1925.

gen.<sup>11</sup> Following such fixation, subcutaneous, intravenous or intragastric administration of the homologous antigen is followed by an acute inflammatory reaction.<sup>12</sup> Moreover, passive local sensitization of the gastrointestinal tract in experimental animals and of the rectum in man<sup>13</sup> indicates that the colon may properly be classed as a shock organ.

Another school of thought holds that a large proportion of the cases are of psychogenic origin.<sup>14</sup> Emotional disturbances operating through the vegetative nervous

TABLE 1.—Duration of Observation (Eighty-Five Cases)

Months	Cases
18-23.....	12
24-35.....	22
36-47.....	17
48-59.....	11
60-71.....	20
72-78.....	3

system are believed to produce hyperperistalsis and surface digestion of the mucosa of the colon.

Studies previously reported<sup>15</sup> have led to the belief that conditioned deficiency disease constitutes an important secondary factor in the mechanism of many cases of chronic ulcerative colitis.

It is inevitable that these differing concepts should lead to a variety of different forms of therapy. These have been principally directed to the effort to eliminate infection. Vaccines of various types, antisera, bacteriophage, irrigation with many types of antiseptic solutions, irradiated oils, irradiated transfusions and the exhibition of adsorptive agents such as fullers' earth and bismuth all have had their enthusiastic proponents. The antibacterial approach to the problem has even determined the time for surgical intervention and the procedure to be performed. Appendicostomy, cecostomy and colostomy have been carried out many times in the belief that by facilitating through and through irrigation cure might be obtained.

TABLE 2.—Extent of Pathologic Condition (Eighty Cases)

	Cases
Rectum only.....	4
Distal to sigmoid.....	21
Distal to splenic flexure.....	17
Distal to hepatic flexure.....	10
Entire colon.....	26
Proximal to sigmoid only.....	2

The same conflict of opinion exists with respect to prognosis. For example, Hurst<sup>16</sup> believes that a large majority of patients irrespective of the severity of the disease may ultimately lead a life of normal activity

free from recurrences. Paulson,<sup>17</sup> on the other hand, considers permanent cure only a remote possibility in all but the exceptional cases. Frequently statements of results of therapy are based on relatively brief periods of observation and subsequent reports of the subjective phenomena noted by the patient. Despite the optimistic statements there is a deeply rooted belief in the profession that therapy is inefficient and that ulcerative colitis, once established, becomes a chronic disease exhibiting recurring periods of activity and quiescence.

The studies here reported were undertaken in the belief that continuous investigation of a group of cases over a prolonged period might yield information of value.

## METHODS

Proctoscopy was done on each patient at every visit, and cultures were taken directly from the rectal or rectosigmoidal mucosa on plates of MacConkey agar, eosin-methylene blue agar and desoxycholate agar. From slightly more than half of the patients tall tubes of Rosenow's glucose brain broth have been inoculated and studied by the Bagen technic.<sup>18</sup> Recently anaerobic cultures have been made from a small proportion of the group.

The distribution of the lesions has been determined by means of the sigmoidoscope and a barium sulfate enema. Motor physiology of the intestine has been

TABLE 3.—Fractional Gastric Analysis (Seventy-Two Cases)

	Cases
Normal acid curve.....	38
Hypocidity.....	27
Anacidity.....	12

studied by twenty-four and forty-eight hour x-ray films of the abdomen after oral administration of the barium compound. During the test period the patients receive the usual dietary, but cathartics and sedatives are withheld.

Fractional gastric analyses have been performed with histamine stimulation.

Allergic studies were done by the test diet method and the repeated addition and withdrawal of suspected foods.

Owing to financial obstacles and difficulties of cooperation, it has not been possible to make complete observations in all cases of the group.

## MATERIAL

Eighty-five cases of chronic ulcerative colitis have been studied for periods varying from eighteen months to six and a half years. All but twelve have been followed for two years or more. Fifty-one have been studied for three years or more. These patients have been drawn from dispensary, hospital and private practice in New York City. They constitute a selected group in the sense that only those cases frequently examined throughout the period of observation and only those studied for a minimal period of eighteen months are included.

The extent of the pathologic condition in the colon as shown by proctoscopy and x-ray examination was

17. Paulson, Moses: The Present Status of Idiopathic Ulcerative Colitis, with Especial Reference to Etiology, J. A. M. A. 101:1087-1092 (Nov. 25) 1933.  
18. Bagen, J. A.: Personal communication to author, 1937.

11. Opie, E. L.: The Significance of Allergy in Disease, Medicine 15: 489-509 (Dec.) 1936.

12. Seegal, David, and Seegal, Beatrice C.: Local Organ Hypersensitiveness: III. Further Observations on Its Experimental Production in the Rabbit Eye, J. Exper. Med. 54: 249-263 (Aug. 1) 1931; IV. Inflammation Produced in the Actively Sensitized Rabbit Eye by the Introduction of Homologous Antigen into the Gastrointestinal Tract, ibid. 54: 265-269 (Aug. 1) 1931.

13. Walzer, Matthew; Gray, Irving; Straus, H. W., and Livingston, Saul: Studies in Experimental Hypersensitiveness in the Rhesus Monkey: IV. The Allergic Reaction in Passively, Locally Sensitized Abdominal Organs, J. Immunol. 34: 91-95 (Feb.) 1938. Gray, Irving, and Walzer, Matthew: Studies in Mucous Membrane Hypersensitiveness: III. The Allergic Reaction of the Passively Sensitized Rectal Mucous Membrane, Am. J. Digest. Dis. & Nutrition 4: 707-711 (Jan.) 1938.

14. Sullivan, A. J.: Psychogenic Factors in Ulcerative Colitis, Am. J. Digest. Dis. & Nutrition 2: 651-656 (Jan.) 1936.

15. Mackie, T. T.: Ulcerative Colitis: II. The Factor of Deficiency States, J. A. M. A. 104: 175-178 (Jan. 19) 1935.

16. Hurst, A. F.: Prognosis of Ulcerative Colitis, Lancet 2: 1194-1196 (Nov. 23) 1935.

determined in eighty-five cases. The entire colon from the cecum to the rectum was affected in twenty-six. Involvement distal to the splenic flexure and distal to the sigmoid comprises the next largest groups. In two cases the lesions were limited to that portion of the colon proximal to the sigmoid flexure.

Fractional gastric analysis with histamine stimulation was performed in seventy-two patients. Disturbances of gastric secretion were found to be not uncommon, particularly in the severe cases. Anacidity was present in twelve and hypoacidity in twenty-two.

TABLE 4.—Colon Motor Rate (Forty-Two Cases)

	Cases
Normal motor rate.....	10
Hypermotility.....	11
Hypomotility.....	21

The profuse diarrhea and pain so common in the severe case is attributed to hyperperistalsis and hypermotility of the intestinal tract. This is by no means always the fact. Twenty-one of the forty-two cases examined revealed hypomotility in association with frequent evacuations, abdominal cramps and tenesmus. In these instances there is definite and often prolonged delay of forward progress of the barium in the proximal half of the colon. Occasionally I have observed this delay to extend over ninety-six hours. Thus there may exist the paradox of marked constipation accompanying what seems to be a profuse diarrhea. The exhibition of sedatives and antispasmodics in such a situation merely aggravates an already abnormal condition. Hypermotility, with complete evacuation of the barium sulfate meal in twenty-four hours, occurs less often. The importance of determining which of these two mechanisms is operative in a given case is self evident. Further reference will be made to this in the discussion of therapy.

The bacteriologic studies have not revealed a high incidence of any recognized single pathogenic organism. The flora varies greatly from case to case and in the same case at repeated observations. Unidentified strains of Salmonella have been recovered in many instances. Their pathogenicity has not been investigated. Strains of Shigella dysenteriae have been isolated in twenty-one of the group. The Morgan bacillus No. 1 is likewise not uncommon, and beta hemolytic streptococci have been recovered in certain of the cases.

Recently the bacteriologic investigations have been amplified to include routine use of the Rosenow glucose brain broth with the technic prescribed by Bargen. Forty-seven cases have been studied. Gram-positive diplococci have been recovered from thirty-five. None of these conformed to the cultural criteria and heat resistance test described as characteristic of the "diplococcus of ulcerative colitis." Only one strain conformed to a type strain originally obtained from the Mayo Clinic. It did not agree, however, with two other type strains obtained from the same source.

The sugar fermentations, heat resistance and morphology observed in the diplococci that I have recovered permit their classification only as members of the Streptococcus faecalis group.

Anaerobic cultures have only rarely yielded Bacterium necrophorum.

Prolonged study of these cases has repeatedly demonstrated that a factor of allergy participates in the mechanism of many cases of chronic ulcerative colitis. The frequent association of infection of the upper respiratory tract with recurrence of activity of the disease or with increased severity is well known. On several occasions I have had the misfortune to witness a sudden increase in severity following immediately on an overdose of autogenous vaccine which produced marked local and systemic reaction. Particular foods likewise frequently play a similar role.

The recognition of food allergy in these cases necessitates use of the test diet method of study. Cutaneous tests yield misleading information. Both false positive and false negative reactions are obtained. It is frequently necessary to repeat the test diet studies in order to demonstrate the mechanism in a given patient. Negative results at one time may give way to clearcut and predictable response to the successive exhibition and withdrawal of a particular food a few weeks or months later. The reactivity of the colon therefore exhibits a phasic variation in this respect, apparently corresponding to successive periods of sensitization and desensitization. In some instances evidence of food allergy is obtainable during periods of activity of the disease. In others this factor is demonstrable only in the early stages of recurrence. The following case abstracts illustrate these points:

CASE 77.—The patient, first seen in January 1935, gave a history of continuous diarrhea with bloody mucus and pus since the autumn of 1930. A variety of methods of treatment had been used with little or no improvement.

At the time she came under my observation she was having from four to six liquid stools a day containing considerable amounts of blood and mucus. There was obvious loss of weight and moderate anemia. Proctoscopic examination revealed a diffusely inflamed, thickened, pitted and bleeding mucous membrane extending to the limit of visualization in the rectosigmoid.

TABLE 5.—Bacteriologic Observations (Eighty-Five Cases)

	Cases
Salmonella.....	45
Unidentified.....	40
Paratyphosus B.....	4
Paratyphosus A.....	1
Shigella dysenteriae.....	21
Flexner.....	14
Sonne-Duval.....	6
Shiga.....	1
Bacillus morganii no. 1.....	16
B. faecalis alkaligenes.....	15
Beta hemolytic streptococci.....	14
B. proteus.....	14
B. pyocyaneus.....	12
B. coli anergenes.....	11

A barium sulfate enema showed no evidence of pathologic change proximal to the sigmoid. Cultures from the rectal mucosa yielded large numbers of beta hemolytic streptococci. These were not present in the pharynx.

No history of allergic disease or known food sensitization could be obtained from the patient or her family. Intracutaneous tests with many antigens gave negative results except to coffee, tea, pea, carrot, apple and goat.

Autogenous vaccine failed to produce either subjective or objective improvement.

A milk-free diet was started February 8, with prompt subjective improvement. Stools were reduced in number, mucus was much diminished and bleeding practically ceased. By March 7 the stools had dropped to an average of from two to four in twenty-four hours. Blood and mucus were absent except on two occasions immediately after she had taken orange

juice, which was then omitted. Proctoscopic examination revealed a much less acutely inflamed mucosa which did not bleed.

Milk and milk products were added to the diet at this time. Forty-eight hours later considerable amounts of mucus and blood reappeared and continued for two days after the milk-free diet was resumed. This was continued. By June 25 the patient was symptomatically well and proctoscopic examination revealed a mucosa which was normal save for slight thickening and scarring.

CASE 71.—The patient was first seen in May 1936 when he was seriously ill in the hospital. A positive family history of allergy was obtained. Proctoscopic examination revealed a characteristic picture, and a barium sulfate enema demonstrated an advanced ulcerative colitis extending from the hepatic flexure to the rectum. For two and a half months his condition remained precarious. A moderately severe deficiency disease complicated management. Test diets gave negative results. Finally forced feeding by gavage was resorted to, a synthetic diet containing milk and eggs being used. He was discharged from the hospital August 28 on a general diet, in excellent condition and averaging from two to three stools each twenty-four hours.

October 9 he reported that milk, orange juice and spinach caused increased looseness of the stools. This observation was confirmed by test diets, and the offending foods were omitted.

During the autumn of 1936 he remained in good condition. Proctoscopic examination revealed scattered small follicular

Secondary or conditioned deficiency disease has occurred as a complicating factor in forty-six of the cases. It appears to be the expression of the combined deficit of a number of essential factors. Lowering of the plasma proteins and inversion of the albumin-globulin ratio is not uncommon. The blood calcium is frequently below normal levels. The vitamin A and vitamin C values are often low, and it is probable that certain of the other vitamins are similarly affected.

These mixed deficiency states appear insidiously and gradually assume increasing significance. They may play a most important role in the course of the disease and in the more severe cases may determine the outcome. Recognition of this complication and intensive therapy is essential. The following case illustrates certain of these problems:

CASE 67.—The patient was admitted to the hospital in February 1936 with a history of recurrent attacks of colitis since 1929. In the autumn of 1935 a severe and progressive recurrence developed. During the three weeks prior to admission she had been on a diet low in vitamin C. At the end of this period a series of massive intestinal hemorrhages occurred and the red blood cell count fell to two million. The temperature was elevated and septic. The skin was dry and harsh, and the tongue was beefy red. The abdomen was markedly distended and tender on palpation. There was constant severe abdominal pain. The stools varied from twenty to thirty in twenty-four hours, many of them passed involuntarily, and they contained large amounts of mucus and blood.

The diet was modified immediately and supplemented by 250 mg. of crystalline vitamin C intravenously each day. Determination of vitamin C in the blood and urine unfortunately could not be carried out. Critical cessation of bleeding occurred at the end of the first week. During the ensuing weeks extreme anorexia constituted the major problem and undoubtedly was an important contribution to the subsequent developments.

The anemia was treated at first by three transfusions and then by iron, which brought about satisfactory blood regeneration up to the first week of March.

At this time the tongue became acutely inflamed, serpiginous ulcers covered with grayish slough appeared, and there were numerous aphthous ulcers in the buccal mucosa. The sloughs on the tongue separated after a few days, leaving a smooth, inflamed surface. At this time a symmetrically disposed eczematoid rash appeared on the lower part of the thighs, the anterior aspect of the knees and over the lower legs. She became markedly edematous, and free fluid was present in the abdominal cavity. The anemia became macrocytic, response to iron ceased and megaloblasts were present in the stained blood films.

Gavage feeding of a synthetic diet high in protein and vitamins was instituted. Large daily doses of unconcentrated liver extract (Lilly) were given parenterally.

The anemia and the lesions on the tongue, mouth and skin responded promptly. The subsequent course was uneventful and the patient was discharged from the hospital April 18.

# COMMENT

These observations have led me to certain conclusions concerning the mechanism of chronic ulcerative colitis. The evidence so far available does not justify the hypothesis that the disease is a specific infection resulting from the primary action of a single specific micro-organism. On the contrary, there is much evidence to indicate that it may be initiated by any one of a number of bacteria, known to be pathogenic and known to produce inflammatory lesions in the colon. Once the mucosal barrier has been broken by such an agent, secondary infection necessarily occurs. The secondary invaders will naturally include certain of the bacteria present in the colonic contents. Sections of colon removed surgically or at autopsy and stained for

TABLE 6.—Incidence of Food Allergy (Sixty-Seven Cases)

Results of Test Diet Studies	History of Allergic Disease, Patient or Family	Previous Food Idiosyncrasies
Evidence of active food allergy, 44 cases..	12	23
Questionable, 7 cases.....	4	3
Negative, 16 cases.....	..	..

ulcers and a hyperemic mucosa. From October through December *Shigella dysenteriae* Flexner was isolated on six occasions in almost pure culture.

An acute recurrence of active colitis developed in January 1937 after administration of autogenous Flexner bacillus vaccine. The patient was again hospitalized for twelve weeks. Milk, wheat, egg and spinach seemed definitely to increase symptoms at this time. Definite improvement occurred on the test diets. He was discharged in April and, contrary to advice, resumed the ingestion of milk, which he tolerated without apparent difficulty until August, when the stools increased in number and became looser, and mucus and blood reappeared. Immediate improvement occurred following the withdrawal of milk and milk products from the diet, even though the patient strenuously objected to this measure.

These two cases illustrate the varying response to dietary study in the different phases of the disease. The second case emphasizes the necessity for repeated search for a possible factor of food sensitization.

Satisfactory allergic studies were completed in sixty-seven cases. Classification was based on the subjective phenomena reported by the patient and more particularly on the appearance of the mucous membrane of the rectum and the rectosigmoid at repeated proctoscopic examination after each change in diet. Clinical evidence of active food allergy was obtained in forty-four cases. In seven others the evidence was equivocal. A history of allergic disease in the patient or in the patient's family was not a common finding. Idiosyncrasies to certain foods have been noted by about half of the cases. In the order of frequency, the foods most commonly at fault were milk, egg, orange, wheat, spinach and tomato.

bacteria reveal gram-negative bacteria in the more superficial portions of the affected tissue and gram-positive organisms in the deeper levels. Under such conditions it is not remarkable that conflicting observations have been recorded, nor is it remarkable that special methods will yield certain types of bacteria in significant numbers. Both types of observation are factual. Unfortunately they have tended to create dis-sension rather than progress.

The phenomena of the disease appear to result from the combined action of a number of factors. There is infection, probably always mixed in character, of the affected portion of the wall of the colon. Both the secretory and the motor physiology of the gastrointestinal tract are adversely and variously affected. Sensitization of the colon to foreign protein of bacterial and dietary origin plays an important role in the mechanism of relapse and activity of the disease. Not infrequently secondary deficiency states occur and assume major clinical importance.

#### TREATMENT

The medical management of chronic ulcerative colitis must be based on this complex mechanism and it must be guided by the phenomena observed in the particular case. In the past the greatest emphasis has been placed on antibacterial measures. This originated in the concept that ulcerative colitis is a simple infection and that its effects, both pathologic and physiologic, are restricted to the colon. This hypothesis is no longer tenable. The great variety of antibacterial measures advocated bears mute but impressive testimony to the inadequacy of all.

Disturbances of normal physiology must be compensated. Hydrochloric acid in amounts up to 4 cc. with meals is of definite value in the presence of anacidity. It tends to control distention and flatulence and to curtail the diarrhea. Sedatives such as phenobarbital and at times opium derivatives are useful in the presence of a hypermotile colon. They are contraindicated in those cases presenting a slow colon motor rate. In the latter the number of stools and the amount of pain are usually reduced by a properly adjusted daily dose of a saline cathartic and large fluid intake.

Adjustment of the diet to the needs of the patient is essential. A high protein low carbohydrate diet is better tolerated than the conventional high carbohydrate "colitis diets" traditionally in use. The importance of repeated investigation of the possibility of food allergy by the test diet method cannot be overemphasized.

The vitamin and mineral intake must be maintained at levels above the requirements of the normal individual. This necessitates supplementing the diet by the addition of special sources. Such supplements are essential during periods when the restricted test diets are in use. A constant watch must be kept for the early signs of deficiency disease and when evident they must be strenuously treated.

Autogenous vaccines, if recognized pathogens have been recovered on culture, appear to be helpful when used in conjunction with the other methods of treatment. Evaluation of the effects of vaccine therapy, however, is often difficult, particularly in view of the psychic effect on many patients who strongly believe in their efficacy. On theoretical grounds the rationale for the use of antisera seems less well grounded. I have not been impressed by the results of bacteriophage treatment in this disease.

Certain general measures are applicable. Definite foci of infection should be appropriately treated. Education of the patient to cope more successfully with his psychologic problems is frequently important. The effort to achieve formed stools, especially by the use of bismuth, is ill advised, since it adds to the already complex mechanism—the factor of mechanical trauma to the inflamed mucosa. I believe that the stools should be kept liquid or semiliquid until healing is complete.

What results are to be anticipated from medical management? It is unfortunate that the word "cure" has been used in connection with chronic ulcerative colitis. Too frequently it appears as a chronic progressive disease exhibiting periods of spontaneous activity and quiescence. Fifty-one of the patients have had recurrences or have shown continuous activity of the colitis with failure to respond satisfactorily to treatment. It is impossible to say that after any given period of freedom from activity the disease will not recur. In this respect it resembles the problem of pulmonary tuberculosis. It is impossible to be certain from the patient's symptoms or lack of symptoms that healing has actually occurred unless confirmation is obtained by both the sigmoidoscope and the x-rays.

TABLE 7.—Results of Treatment in Eighty-Five Cases

	Cases
Apparently arrested.....	23*
Less than 12 months.....	3
12-23 months.....	6
24-35 months.....	10
36-47 months.....	2
48 or more months.....	2
Improved.....	44
Unimproved.....	13
Died.....	5

\* Four cases treated surgically.

In this respect also the problem resembles that of tuberculosis. Consequently it seems most desirable to borrow from the terminology of the latter disease and to substitute the term "apparently arrested" for "cured."

Twenty-three of the cases are apparently arrested, forty-four are definitely improved but not healed, thirteen are unimproved and death occurred in five.

#### SURGERY

Prognosis in the individual case depends necessarily on the extent of irreparable damage to the colon and on identification and control of the factors operating to maintain activity of the disease. When extensive anatomic changes have occurred it is vain to hope for restoration to normal. Many such cases constitute serious problems of management. The complications resulting from chronic sepsis are common and, as was the case in two of my fatalities, these complications may lead not only to chronic invalidism but to death of the patient.

In the last few years there has been an increasing tendency to include radical surgery among the available therapeutic measures. The selection of cases and the decision as to when to resort to operative intervention imply the necessity for joint medical and surgical study and supervision both before and after operation. The detailed management of these problems should be carried out under the direct supervision of the senior physician and the senior surgeon of the group. In conjunction with Dr. Henry W. Cave such a detailed and combined approach has been made an



colon. It is also wise not to make the loop colostomy but to divide the bowel and its mesentery for some distance so as to try to obviate the jumping over of the infection. I need not say that the object is to put the diseased bowel completely at rest. There is considerable discussion regarding the value of irrigation of the distal loop. I believe it has a distinct value and cannot be duplicated by enemas without colostomy.

If the disease has begun to invade the transverse colon, of course, there is no alternative except to do an ileostomy or to depend entirely on medical management in the hope of arresting the spread of the process. The choice depends on the condition of the patient. If there is no improvement after adequate medical treatment, ileostomy is advisable early rather than late; for, if the disease process is arrested, the ileostomy may be changed to a colostomy after a long period, provided the process has not extended into the ascending colon.

If the entire colon is involved and the patient does not respond to medical management, ileostomy becomes imperative and the condition of the patient spells the optimal time. In the performance of ileostomy it is again necessary to divide the bowel at that point and institute through and through irrigation. The future course depends entirely on the convalescence of the patient. If he improves, gains weight, has no symptoms of toxic absorption and is not troubled much with frequent emissions from the rectum, I do not think it is necessary to subject him to colectomy. On the other hand, if he still seems toxic and does not gain weight, I think colectomy is indicated. If colectomy is done, it is best to use graded procedures, employing two or three operations as outlined by Rankin, Cattell and others.

In a review of 137 cases of chronic ulcerative colitis which were seen at the Cleveland Clinic in the past ten years, roentgen examinations showed that fully one half were limited to the rectum or left half of the colon. Many of these have eventually gone on to involve the entire colon in spite of all treatment. I would interpret that by picturing an invasion of upper segments of the bowel with each recurrent attack.

This brings me to the question Is it not possible for this section to outline what it would call adequate treatment? Then could not sufficient time be taken to try out these different treatments to determine which were most satisfactory or which failed, even though this might be a year or even two years? If we could know that certain therapy under certain circumstances would fail to give relief, why delay surgery? My plea is for surgical intervention while the lesion is limited to the left side. It should be remembered that, following surgical treatment, the patient should not be abandoned. Medical treatment is just as necessary at this time as at any other. If a specific should be introduced, the colostomy could be closed. If further surgery is necessary, it would involve removal of only the left half of the colon instead of the entire colon and the patient would, in the end, have a colostomy instead of an ileostomy.

The segmental variety, viz., that in which only a part of the colon may be attacked, the ascending, transverse or descending colon or any combination of these, constitutes about 5 per cent of the entire group. Here again surgical treatment should not be delayed too long for fear that the entire colon will become involved.

## PROGNOSIS OF ULCERATIVE COLITIS

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Although the literature contains many references to the etiology, treatment and complications of so-called idiopathic ulcerative colitis, there has been little written concerning the natural history and the final outcome of cases of this disease. Such a study is essential before any definite evaluation of specific therapeutic measures can be made. In an effort to obtain information regarding the prognosis in this type of ulcerative colitis we have reviewed our records of the past twelve years and from 100 cases have selected sixty-six the records of which are complete. These have either terminated fatally while under observation or have been followed for a period of more than three years. The thirty-four cases which were not used lacked complete follow-up data. Twenty additional cases of various types of colitis were discarded because of atypical manifestations or incomplete diagnostic records. This group included amebic disease, tuberculous colitis, bacillary dysentery, regional colitis, ulcerative proctitis with positive Frei tests and other types of colitis which could not be classified definitely. This method of selection probably does not give an accurate cross section of the prognosis of the disease, since it is likely that many of those who failed to return for follow up are patients with the milder types of disease who have spontaneously improved, while those who have died under observation and those followed over a period of years probably were the more severely ill patients.

### DIAGNOSIS

All patients included in this series had a history of varying degrees of diarrhea, passage of blood, mucus or pus in the stools, abdominal cramps, febrile reactions and other signs of active disease. The diagnosis was established and the course followed in all cases by sigmoidoscopy and x-ray examinations. Only typical cases were accepted; such as those showing, by sigmoidoscopy, diffuse mucosal involvement with multiple military ulcerations, either active or healing, with pitting and an easily traumatized mucosa. Polypoid hyperplasia or actual polyposis was frequently seen. Cases presenting an atypical appearance of the rectal or sigmoidal mucosa were discarded. All cases were studied with the barium sulfate enema with one exception, an acute fulminating infection in which death occurred on the seventh day. While typical x-ray changes—narrowing, shortening and mucosal mottling—were not deemed necessary for the diagnosis, such changes were seen in most cases. Amebic colitis was ruled out by direct inspection of the intestine and numerous microscopic examinations of smears from the ulcerated areas and also repeated stool studies. Cultures were taken from all patients, many on numerous occasions, with special mediums to rule out *Bacillus dysenteriae* infection. Serum agglutination tests for *B. dysenteriae* were

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done on all hospitalized patients. In the past five years many of the patients have had Frei tests; those with positive results have been eliminated from this series. No attempt to isolate the virus of venereal lymphogranuloma from intestinal discharges has been made.

FINAL CLASSIFICATION

The final status of each patient has been determined by the subjective complaints and objective examinations, including endoscopy and x-ray examination. Of the sixty-six patients fifty-two (79 per cent) were seen by one of us at the last visit. In nine instances (13.5 per cent) the final opinion was based on the report of the referring physician, while five patients (7.5 per cent) reported by letter. These final reports were compared with the original reports and the results tabulated as follows:

1. Death: Those dying (a) of the disease, (b) following operation or (c) from intercurrent causes.
2. Progression: Those showing continuance of or increase of symptoms with extension of x-ray involvement or occurrence of complications.
3. No change: Those showing continuance of symptoms with no significant change in the endoscopy or x-ray examination.
4. Slight improvement: Those with (a) less active symptoms or more prolonged remissions, (b) general clinical improvement with or without objective change or (c) objective improvement with little symptomatic change.
5. Definite improvement: Those having (a) few or intermittent symptoms, (b) definite healing but with remaining evidence of disease by sigmoidoscopy (pitting, polyposis, easy trauma) or (c) x-ray regression.
6. Remission: Those with (a) complete disappearance of active symptoms, (b) normal appearing mucosa

TABLE 1.—Treatment

	Cases	Per Cent
Blood diet	66	100
	51	77
	49	74
Autogenous vaccine.....	48	73
	47	71
	46	70
	37	56
Calcium.....	36	54
Iodine.....	20	44
Sedatives.....	27	40
Opiates.....	23	38
Ultraviolet irradiation.....	23	38
Parathyroid extract.....	21	35
Transfusions.....	21	32
Removal of focal infection.....	20	30.5
Antidysentery serum.....	19	29
Antilameche therapy.....	10	15
Bargen's vaccine.....	9	13.5
Bacteriophage.....	7	10.5
Allergic therapy.....	7	10.5
Potassium permanganate instillations.....	3	4.5
	3	4.5
	2	3
	2	3
Bargen's serum.....	2	3
Radolatum.....	2	3
X-ray.....	1	1.5
Oxygen.....	1	1.5

\* Para-thioresol, McNeil Laboratories, Inc., Philadelphia.

except for possibly slight pitting or residual non-inflamed polyps, (c) lack of x-ray evidence of activity although narrowing or shortening might remain. The remission was at least a year in duration before being so classified. We realize the inaccuracies of such a classification but believe it to be the best for our purpose.

TREATMENT

Since it has been our practice to use many therapeutic measures (table 1) concomitantly, no attempt has been made to draw definite conclusions regarding the value

of any single therapeutic procedure. The accompanying table indicates the frequency with which various measures were used. Particular efforts were made in every instance to keep the patient's morale at the highest possible level. This form of psychotherapy was considered most important.

Surgery was resorted to in fifteen cases (23 per cent) and included twelve ileostomies, two cecostomies and one colectomy.

DESCRIPTION OF CASES AND RESULTS

The cases have been grouped according to the course of the disease into the following types (table 3):

TABLE 3.—Analysis of Results

	Cases	Death, per Cent	Progress or No Change, per Cent	Improved, per Cent	Remission, per Cent
Sex					
Females.....	34	35	15	23	27
Males.....	32	22	22	31	25
Age of onset					
10-19.....	16	18.7	31	25	25
20-29.....	22	32	4.5	36	27
30-39.....	16	31	25	25	18
40-80.....	12	33	17	17	33
Duration of symptoms					
Less than 1 year.....	24	42	12.5	25	20
1-2 years.....	12	17	25	33	33
2-5 years.....	16	37.5	18.7	12	31
5-10 years.....	9	11	11	44	33
10 plus years.....	5	0	40	40	20
Extent of x-ray signs					
None.....	14	21.4	14.5	35.7	28.5
Rectum and sigmoid.....	18	16.6	22	22	39
Left colon.....	22	45.4	18.2	18.2	18.2
Entire colon.....	11	18.2	18.2	45.4	18.2
Type of disease					
.....	8	62.5	0	12.5	25
.....	24	33	29	29	8
.....	34	17.6	14.7	29.4	39

chronic relapsing, chronic continuous and acute fulminating. No further classification was attempted because of the extremely variable course of the individual case. The association of fever or toxic manifestations and the relative severity of subjective complaints, such as the number of stools, relative amounts of pus and blood and the presence of abdominal pain, seemed too variable for accurate analysis. The sigmoidoscopic picture also was so variable that no definite segregation of types seemed possible.

In a great majority of our cases the disease ran a chronic course. Thirty-three (50 per cent) were of the chronic relapsing type with irregular remissions and relapses, many presenting a seasonal relationship (spring and fall); in twenty-five (38 per cent) the disease had a chronic continuous course, and eight (12 per cent) were of the acute fulminating variety. This incidence of acute fulminating cases is higher than in other reported series and may be accounted for by the fact that most of our patients were seen in the gastrointestinal clinic of a general hospital associated with a teaching institution in a large city. It is likely that more acute cases find their way to such a clinic than to clinics farther removed from centers of population, such as the Mayo Clinic, Ruthin Castle, or the New Lodge Clinic attended by Hurst.<sup>1</sup> In our experience the acute fulminating type of disease results in death in a relatively short time (from one week to three months) or goes on to practically complete recovery. Five of our eight patients died and four were operated on. None of the patients who recovered had been

1. Hurst, A. F.: Prognosis in Ulcerative Colitis, *Lancet* 2:1194-1196 (Nov. 23) 1935; Ulcerative Colitis, *Guy's Hosp. Rep.* 85:317-355 (July) 1935.

subjected to operation. The best chance of complete remission is in the chronic relapsing type. This occurred in 39 per cent and definite improvement or remission occurred in about 70 per cent. No change was noted in about 15 per cent of this group, while about 15 per cent died. The chronic continuous type of disease resulted in death of one third with an additional 29 per cent having poor results. Only 37 per cent gave a satisfactory response and of those only 8 per cent had a sustained remission.

## SEX

The distribution between the sexes was almost equal, there being thirty-four females and thirty-two males. There were twenty-eight of Jewish extraction and three Italians. Five Negro patients were included, all females; the Frei test was negative in three of these but was not done in two earlier cases. As will be seen in table 3 and chart 1, there was no significant difference in the course of the disease in the two sexes except for a slightly higher mortality rate in females.

## AGE

The greatest number of cases appeared in the third and fourth decades, 65 per cent being between 20 and 39 years of age. With anamnesis to determine the age of onset of the disease—a somewhat inaccurate procedure, but of more value in a study of the natural history than the age at which the patient first came under observation—it appears that 82 per cent of the patients first had symptoms of the disease between the ages of 10 and 49. Only 7.5 per cent dated the onset at an age over 50 years (table 2). Although the group is too small for statistical analysis, it is of interest that

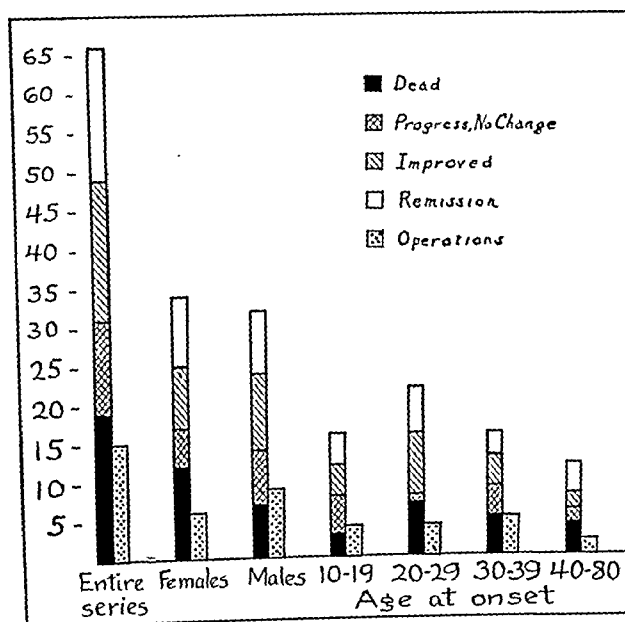


Chart 1.—Results in entire series, showing proportion of patients operated on.

the disease began in the teens more frequently in males than in females (10:6) but that in the years between 20 and 29 there was a much greater incidence in females (16:6). The males again lead in the next decade (10:6). Those favoring a psychogenic pathogenesis of ulcerative colitis might infer that the teens offer more psychic difficulties to the male sex, while the twenties offer the greater adjustment problems to the female. The age of onset seems to make little difference in the

prognosis, although the mortality rate was somewhat lower in those whose disease began between the ages of 10 and 19 years.

## DURATION OF SYMPTOMS

The duration of symptoms when seen by us varied from a few days to more than seventeen years. Twenty-four patients (36.3 per cent) gave histories of less than one year's duration, twelve (18 per cent) from one to

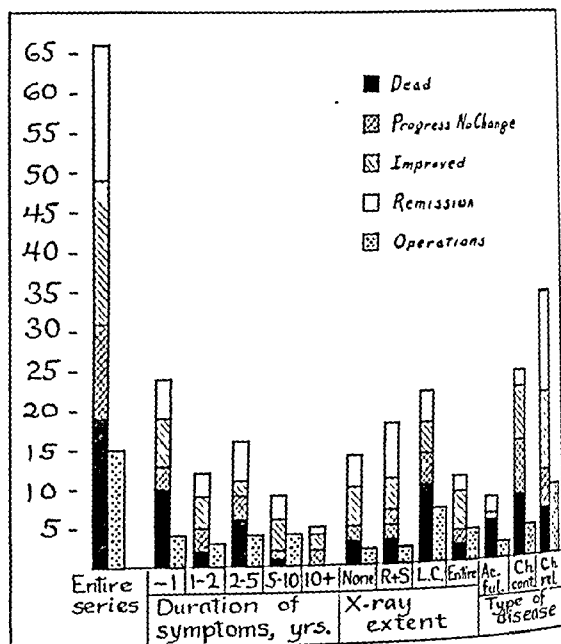


Chart 2.—Duration of symptoms, extent of involvement determined by x-ray examination and type of disease in entire series. None indicates no involvement; R & S, involvement of rectum and sigmoid; L. C., involvement of left colon; entire, involvement of practically the entire colon; Ac. Ful., acute fulminating course; Ch. Cont., chronic continuous course; Ch. Rel., chronic relapsing course.

two years, sixteen (24 per cent) from two to five years, nine (13.6 per cent) from five to ten years and five (7.5 per cent) ten years or more. It is of interest that these five patients are all living and at present have had the disease for more than twenty years, the longest time being twenty-seven years. The shortest total duration of the disease was two weeks in a patient who died of a peculiarly virulent fulminating attack.

The highest mortality and lowest rate of improvement were seen in those giving a history of symptoms of less than one year. Those with histories of over ten years' duration are all alive, but only one of the five has had a remission. Regardless of the duration, the incidence of remissions was between 20 and 33 per cent.

A possible explanation of the high mortality figures in this series is the inclusion of eight cases of the acute fulminating type which carried a mortality rate of 62.5 per cent. These five rapidly fatal cases represent 7.5 per cent of the total group. In Bergen's<sup>2</sup> recent figures only twenty-one of 871 cases, or 2.4 per cent of the total group, presented this fulminating type. It is difficult to obtain from other papers the incidence of these acute cases; hence comparisons are impossible.

## EXTENT OF X-RAY INVOLVEMENT

Classification as to extent of involvement of the colon as determined by barium sulfate enema examination also has been attempted. Narrowing, shortening, rigid-

2. Bergen, J. A.; Jackman, R. J., and Kerr, J. G.: Studies on the Life Histories of Patients with Chronic Ulcerative Colitis with Suggestions for Treatment, *Ann. Int. Med.* 12: 339 (Sept.) 1938.

ity or lack of haustrations, or extreme irritability and irregular mucosal outlines have been considered in this estimation. Since clearcut demarcation is rarely seen, no sharp distinction has been drawn. The cases were divided into four groups (table 3): (1) those presenting no definite x-ray changes, (2) those presenting

TABLE 5.—Final Results

	Cases	Per Cent of Total
Dead.....	19	29
Alive		
Progression.....	4	6
No improvement.....	8	12
Slight improvement.....	7	10.6
Marked improvement.....	11	16.6
Remissions.....	17	25.7
	47	71

involvement of the rectum and sigmoid only, (3) those presenting disease of the left colon (not beyond the midtransverse), and (4) those presenting extension to the right colon or complete colonic involvement. Sixty per cent of the patients showed x-ray changes in the rectum and sigmoid or extension to the left colon, while 21 per cent showed no definite x-ray signs and 17 per cent showed disease of practically the entire colon.

thirty-one (47 per cent) are either dead or not improved, while thirty-five (53 per cent) are improved or in remission (table 5).

The literature<sup>3</sup> contains reports of mortality rates ranging from 9.3 to 40 per cent. It is difficult to compare these figures because of different sources of material and various criteria for classification. The incidence of fulminating disease is apparently higher in our series than in others reported. This undoubtedly has an important influence on our statistics regarding mortality and improvement. An additional factor influencing the final figures is the inclusion of deaths from all causes. Five patients died of diseases not directly related to the ulcerative colitis. These include three cardiovascular deaths, two of which occurred during a remission of the colitis; one suicide of a patient who was somewhat improved after cecostomy, and one death from meningitis secondary to mastoiditis of a patient whose colitis was somewhat improved.

SURGERY

Another factor influencing the results is the frequency with which surgery was attempted during a part of the period covered by this survey (tables 7 and 8). The postoperative mortality, in our experience, has been 42 per cent. Operations were performed

TABLE 8.—Surgical Cases

	Sex	Age	Duration at Operation	Pre-operative X-Ray	Reason for Operation	Preoperative Condition	Operation	Post-operative Condition	Cause of Death	Time
Postoperative fatalities										
Acute fulminating										
J. R.....	♂	39	7 wks.	Entire	Toxemia, bleeding, polyposis	Very poor	Ileostomy	Death	Toxemia	P.O.
P. S.....	♀	17	6 mo.	L.C.	Progression, long relapse	Very poor	Ileostomy	Death	Toxemia	P.O.
Chronic relapsing										
E. H.....	♀	25	5½ yrs.	L.C.	Progression, long relapse	Good	Ileostomy	Death	Volvulus, peritonitis	P.O.
H. G.....	♂	24	4½ yrs.	L.C.	Toxemia, peritonitis	Very poor	Ileostomy	Death	Peritonitis	P.O.
E. F.....	♂	49	8 yrs.	Entire	Long relapse	Fair	Ileostomy	Death	Peritonitis, obstruction	P.O.
C. K.....	♂	34	2 yrs.	L.C.	Toxemia	Fair	Cecostomy	Death	Peritonitis	P.O.
Chronic continuous										
A. M.....	♀	30	15 mo.	Entire	Toxemia, bleeding	Very poor	Ileostomy	Death	Toxemia	P.O.
J. G.....	♂	18	3½ yrs.	Entire	Toxemia, arthritis	Poor	Ileostomy	Death	Perforation, peritonitis	P.O.
Later fatalities in operative cases										
Chronic relapsing										
B. Z.....	♂	44	8 yrs.	L.C.	Long relapse	Fair	Cecostomy	Fair	Suicide	3 mo.
A. C.....	♀	30	6 yrs.	Entire	Long relapse	Poor	Ileostomy	Poor	Iliac phlebitis	1 mo.
Chronic continuous										
R. H.....	♀	22	3 mo.	L.C.	Toxemia, bleeding	Poor	Ileostomy	Fair	Liver abscess	2 yrs.
Living patients										
Chronic relapsing										
A. K.....	♂	40	1 yr.	R&S	Polyposis, bleeding	Poor	Ileostomy	Poor		5½ yrs.
I. P.....	♂	35	{ 6 mo. 3 yrs.	Entire	Polyposis, bleeding	Fair	Ileostomy 2	{ Fair Good		{ 3 yrs. 6 mo.
T. M.....	♀	26	{ 4 yrs. 7 yrs.	{ L.C. Entire	{ Long relapse, arthritis Arthritis	{ Fair Fair	{ Ileostomy Colectomy	{ Fair Fair		{ 6 mo. 6 mo.
Chronic continuous										
W. F.....	♂	43	13 mo.	L.C.	Polyposis, bleeding	Fair	Ileostomy	Fair		4 yrs.

L.C. = left portion of colon.

R&S = rectum and sigmoid.

P.O. = postoperative.

The group showing only involvement of the rectum and sigmoid presented the best outlook; the poorest results were obtained in those with extension to the left colon. Of those with no demonstrable x-ray changes a large proportion had an acute fulminating course, accounting for the high mortality in this group.

SUMMARY OF RESULTS

Forty-seven (71 per cent) of the total group of sixty-six patients are alive and nineteen (29 per cent) are dead. Twelve (25 per cent) of the living patients have shown progression or no improvement in the disease; seven (15 per cent) are slightly improved and twenty-eight (60 per cent) are greatly improved or in complete remission. If the entire group is considered,

in 22.7 per cent of the entire series (58 per cent of the fatal cases). Only 27 per cent of the patients who were operated on have lived (four patients). Two of these are decidedly uncomfortable with their ileostomies, one has improved following ileostomy and one has shown slight general improvement after a colectomy done six months ago.

A further study of the fifteen cases referred for surgery shows that in four instances operation was

3. Reports have been published by:  
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Bargen, J.

attempted as a last resort in extremely ill patients after all other measures had failed to halt the progress of the disease. Four additional patients were poor risks because of toxemia or loss of blood or both; one of this group is living. Six patients were in fair condition at the time of operation but surgical intervention was decided on because of the progressive course of the disease or because of the presence of polyposis, excessive bleeding or complications such as arthritis and perirectal abscess. Three of these patients are living, two

vention. During the past three years only the most extremely ill patients have been operated on. Many who formerly would have been referred for surgery because of the severity of the disease are now being continued on medical treatment. It is our impression that the more conservative plan is decreasing the mortality rate, although sufficient time has not yet elapsed to evaluate results.

#### CAUSES OF DEATH IN NONSURGICAL CASES

There were eight deaths in nonsurgical cases, an incidence of 12 per cent, or 42 per cent of the deaths in the entire series (table 9). The causes were classified as cardiovascular disease three cases, inanition two cases, acute toxemia one case, toxemia of pregnancy with nephritis one case and meningitis one case. Two of these patients did not die directly as a result of the ulcerative colitis. One died of meningitis secondary to mastoiditis. The other died of cardiovascular disease one year after a remission of the colitis. A third patient was practically symptom free for several months until pregnancy and renal damage appeared.

Three patients had the acute fulminating type of disease, two had the chronic relapsing and three had the chronic continuous type. Four of the eight patients were under 30 years of age. Of the four over 30, three were past 50. Three of the four past 30 died of cardiovascular disease; the fourth had an acute fulminating infection the total duration of which was only two weeks; autopsy showed extensive involvement of the entire colon. Seven of the eight deaths in this group occurred in females.

With two exceptions the fatal nonsurgical cases belonged in the short duration group, six of the patients having had the disease less than one year. The two exceptions were the patient who died of meningitis secondary to mastoiditis, having had ulcerative colitis for three years, and a woman aged 65, who died of cardiovascular disease after a remission of the colonic symptoms, which had begun twelve years before.

TABLE 9.—Deaths in Nonsurgical Cases\*

Cause of death	Cases
Cardiovascular disease.....	3
Inanition.....	2
Acute toxemia.....	1
Pregnancy.....	1
Meningitis.....	1
Type of colitis	
Acute.....	3
Chronic.....	2
Continuous.....	3
Age	
10-20 years.....	4
20-30 years.....	1
30-40 years.....	1
40-50 years.....	1
50-60 years.....	1
60-70 years.....	1
70-80 years.....	1
Sex	
Females.....	7
Males.....	1
Duration of disease (onset to death)	
Less than 1 year.....	6
1-2 years.....	2
2-5 years.....	1
5-10 years.....	1
10 plus years.....	1

\* Eight cases; 12 per cent of total; 42 per cent of deaths.

with ileostomies and one with a colectomy; one who had a cecostomy improved somewhat but committed suicide a few months later. The remaining patient was in good condition at the time of operation, but because of persistent symptoms for five months following a five and one-half year intermittent history, surgery was attempted. She died after operation of volvulus and peritonitis.

The causes of postoperative deaths included peritonitis (three cases), obstruction and peritonitis (two cases) and continued toxemia (three cases). Other causes of death in patients who were operated on were liver abscess (one case), iliac phlebitis (one case) and suicide (one case).

Operation (ileostomy) on two patients with the acute fulminating type of disease ended fatally in both. Ileostomy was done in five chronic relapsing cases with four postoperative deaths. Eight operations were done in the chronic continuous group: five ileostomies, two cecostomies and one colectomy. Two patients died following operation, three have died since and three are living.

There seemed to be little relationship between the results of operation and the duration of symptoms, although the highest immediate death rate appeared in those with symptoms from two to five years in duration. The extent of involvement of the intestine as judged by x-ray examination also had little bearing on the results, although the mortality was slightly higher in those with entire colonic involvement.

In view of this experience with surgery we have become more conservative in advising operative inter-

TABLE 10.—Complications

Complication	Cases	Per Cent of Total
Polyposis or polypoid hyperplasia.....	26	33.3
Stricture.....	5	7.5
Arthritis.....	5	7.5
Allergy.....	5	7.5
Perirectal abscess.....	4	6.0
Fistula in ano.....	3	4.5
Perforation of colon.....	1	1.5
Abscess of liver.....	1	1.5

The x-ray changes in the fatal nonsurgical group varied from no change to involvement of the left colon. None showed disease of the entire colon.

#### COMPLICATIONS

The most frequent complication in this series was polyposis or polypoid hyperplasia of the colonic mucosa as seen endoscopically. Twenty-six patients showed this change at some time in the course of the disease. In general, this complication was not associated with any marked change in the outcome, although the rapid development of polypoid hyperplasia in the acute fulminating type of disease was usually accompanied by profuse and persistent bleeding. Some of these attacks ran a rapidly fatal course.

Other complications in the order of their frequency (table 10) were rectal stricture, allergy, arthritis, peri-

rectal abscess, fistula in ano, perforation of colon and abscess of liver. The incidence of syndromes of definite vitamin deficiency was low. No cases of carcinoma were encountered. Allergy was noted in association with five cases, in three of which this condition may have been of some etiologic importance.

## COMMENT

It is to be emphasized that in selecting these sixty-six patients for study extreme care has been used to exclude all cases which did not exhibit the typical picture of so-called idiopathic ulcerative colitis in one of its various stages. The primary requisite was diffuse involvement of the mucosa of the rectum and sigmoid. Cases presenting isolated ulcerations or patchy involvement were not accepted. We have not included cases of right-sided colitis, regional colitis, ileocolitis or regional ileitis or proved venereal lymphogranuloma. It is our impression that much of the literature concerning ulcerative colitis deals with cases in the latter classifications and not entirely with the type of disease we have chosen to discuss. If cases of regional colitis or right-sided colitis and ileocolitis had been included, our operative statistics would have been much more favorable, since in our experience most of these patients do well with surgical treatment.

The estimation of final results in this series was based on actual examination of the rectal mucosa in 80 per cent of the cases, and only those patients who had been symptom free for one year and who showed no sigmoidoscopic evidence of activity were reported as being in remission.

We believe that the type of colitis discussed in this paper is a clinical entity and that it corresponds to the disease described by Bagen as "thrombo-ulcerative colitis." However, the bacteriologic studies on these cases failed to indicate a specific etiology for the disease.

The serious nature of ulcerative colitis is indicated by the mortality and morbidity figures both in the literature and in this series. In general, the methods of treatment seem to have little effect on the statistics, although the use of multiple procedures makes definite conclusions impossible. It has been our experience that no single therapeutic measure has produced striking results in more than an occasional patient. Some patients have responded well to one procedure during one relapse and to another procedure during a subsequent relapse. The entire armamentarium frequently fails to produce favorable results.

Surgical intervention, in our experience, is one of the factors resulting in a higher mortality rate. This is in agreement with the experience at the Mayo Clinic, where over a period of eleven years (1923-1934) the postoperative mortality was slightly over 52 per cent. This cannot be considered a criticism of the surgical technic but indicates a greater need for conservatism in advising surgical treatment in a disease which entails such a high operative risk. We have been agreeably surprised in the past few years to find in several instances in which ileostomy seemed imminently necessary that a sudden improvement occurred without operation. Many of these patients would have been operated on a few years ago. The nonoperative mortality rate has not been appreciably altered by this more conservative plan.

The acuteness of the infection and the resistance of the patient are obviously important factors prognostically. In this series the highest mortality rate appeared

in those patients with short histories, a finding which is at variance with the figures of Crohn and Rosenak<sup>3</sup> and others. This is probably due to the inclusion of a larger number of cases of acute fulminating disease. Patients with mild symptoms of short duration clearly offer the best prognosis, but many of these seen prior to three years ago were not included in our series because of lack of follow-up data. The greatest number of deaths occurred in those having had the disease for six months or less. In most of the fatal cases the disease had an acute febrile, toxic or fulminating course. The patients whose disease had lasted from seven months to a year showed a lower rate of mortality and a greater incidence of improvement or remission. We have been unable to determine any definite factors contributing to the rapidly fatal course of the disease in some instances.

An increase in the mortality rate was noted in those patients having had symptoms for from two to five years. This might be explained by the debilitating effect of the chronic disease and also by the relative number of operations performed in this group in an effort to relieve long-standing symptoms. After five years the mortality figures are fairly low, suggesting the gradual development of a higher degree of resistance. It is of interest that the percentage of improved or cured (?) patients in this group is the highest of any in the series (77 per cent). Patients having had the disease for more than ten years apparently seldom die as a result of it even though followed for many years. Improvement is often seen in these patients with long-standing disease, but remissions are uncommon.

The x-ray appearance of the colon is not a reliable prognostic guide. If the disease is mild and the involvement is superficial, no appreciable x-ray abnormalities are to be expected. In the very acute fulminating cases, pathologic changes in the intestinal wall may not be sufficiently invasive to produce a so-called characteristic x-ray appearance. A "fuzzy" silhouette or diffuse mottling of the intestine after injection of air may be present. The patients with involvement of the rectum and sigmoid as shown by x-ray examination had a higher morbidity but a lower mortality than those with negative x-ray examinations. X-ray evidence of disease of the left colon was associated with the greatest mortality and the lowest rate of improvement. In the patients showing involvement of the entire colon the rate of mortality was not greater than in those with minimal involvement, and improvement or remissions occurred about as frequently as in the patients with negative x-ray evidence. It would appear that acute toxic exacerbations are less prone to develop in patients with definite narrowing of the entire colon. The disease has "burned itself out," leaving a thickened fibrotic tube with very little chance for absorption or further destruction of tissue.

Finally it should be emphasized that the prognosis in any case of ulcerative colitis must be guarded. Some of the most severely ill patients, with extensive involvement, severe and continuous bleeding and symptoms and signs of marked toxemia, may suddenly or gradually show improvement and finally go into a complete remission. In most cases of this type we have been unable to attribute this change to any one specific therapeutic measure. We should like to stress the importance of continuous active treatment, utilizing every measure to maintain nutrition and resistance at the highest possible level.



## CONCLUSIONS

1. So-called idiopathic ulcerative colitis is a serious disease, being associated with a mortality of from 10 to 40 per cent in various reported series.

2. The results in any given series probably depend more on the types of disease included, the time followed and the incidence of surgical procedures than on specific therapeutic measures used.

3. In our experience, no single therapeutic measure is particularly effective in any number of patients. A regimen including a great variety of procedures would seem to offer the best chance of success in any given case.

4. An immediate postoperative mortality of 42 per cent and a death rate of 73 per cent in surgical cases are strong arguments in favor of a conservative attitude toward surgical intervention in this disease.

5. Sex was apparently not an influential factor in the final results.

6. The age of the patient at the onset of the disease seemed to make little difference in the results obtained in this series. Contrary to the general impression, the appearance of the disease after the age of 40 did not improve the outlook materially.

7. The highest mortality rate was found in the acute fulminating type of disease. With the exception of those having had symptoms for from two to five years, there seemed to be a gradual lowering of the mortality rate inversely proportional to the duration of the disease. However, marked improvement was seen less frequently in the very long-standing cases.

8. Better results were obtained in the chronic relapsing than in the chronic continuous type of disease.

9. The extent of x-ray involvement was not a reliable prognostic sign.

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## ABSTRACT OF DISCUSSION

ON PAPERS OF DR. MACKIE, DR. JONES AND DRs. WILLARD, PESSER, HUNDLEY AND BOCKUS

DR. WILLIAM FITCH CHENEY, San Francisco: The incidence of the disease must be greater in Eastern cities than in San Francisco, because the number of cases the authors report are larger than I have seen, and yet my experience has coincided closely with that which they have expressed. I agreed with Dr. Mackie's statement that there is no reliable bacteriologic finding either in cultures, stool cultures or in agglutination tests. The appearances by the proctoscope are similar in one locality as in another, and the x-ray appearance of the colon in any protracted case is the same as demonstrated today. The important point is treatment, and this so far has been of little avail. The various serums, such as the polyvalent, antibacillary serum which Hirsh in London so esteems and Crohn in New York reports favorably on and the ulcerative colitis antistreptococcus serum of Bergen, have failed to give satisfactory results. All the different plans recommended as regards diet, medication and rectal injections we have used, but remissions and exacerbations occur in spite of all. There are certain cases in which surgical operation is inevitable, and perhaps we have waited too long in some cases, but the fault is largely with the patient. They don't like it and they postpone it as long as possible. Dr. Mackie reported one case in which he had remarkable results with concentrated liver extract. We have been using in these cases recently a concentrated liver extract. We have given it intramuscularly three times a week at the outset or more often, if the case is a serious one, twice a week for the next month, and after that in dosage sufficient to control, sometimes once a week, sometimes once in two weeks. There have been eight cases treated in this way during the past year, with what I consider remarkable results. The credit for this work belongs to Dr. Garnett

Cheney, but I speak as an observer and not from hearsay. We have seen improvement in weight, comfort and efficiency, and in bowel condition as shown by the proctoscope; and if we discontinued it we saw a relapse, to be succeeded by improvement when we resumed it, but I agree again with Dr. Mackie that treatment must be continued. He compares the disease to tuberculosis. I would compare it to pernicious anemia in this respect. I realize that the time during which this has been tried is short and the number of cases, eight in all, is few; but at least, after years of experience in these cases, I have never seen anything act as well as this has.

DR. JOHN H. FITZGIBBON, Portland, Ore.: In treating ulcerative colitis, our point of view must be extremely broad. As in the care of peptic ulcer, treatment must be planned over a prolonged period, divided into two parts: the immediate treatment with an attempt to heal the condition, followed by lifelong observation and care to prevent recurrence. The patient must be treated as an individual and there is no way of standardizing methods. Each patient has his idiosyncrasies and responses to treatment. The patient is entitled to know the truth about his condition, but when the truth is presented to him or to his parents, if he is a youngster, it should be presented in an optimistic way. One of the chief difficulties in obtaining good results has been the hopeless attitude on the part of many of the medical profession. Patients or their families frequently come with a hopeless feeling about the disease and they are in a more or less desperate state of mind. This has led to delayed surgery, as Dr. Jones has emphasized. While I agree with Dr. Jones that the high mortality is chiefly because of late operation in the cases which come to operation, I am inclined to favor Dr. Mackie's outline of indications for surgery, which are conservative. Early surgical intervention, in my experience, has been rather unfortunate in several cases. When I have become alarmed and rushed the patient to operation, the mortality rate has been extremely high. On the other hand, when I have watched the patient and done everything possible to maintain his nutrition, vitamin intake and particularly his fluids, the results of operation have been better. Physicians should not feel hopeless about the prognosis. There is nothing more gratifying to a physician than to cooperate with a careful, conservative surgeon and obtain a good result in one of these cases. When we see an individual whose life is absolutely worthless, who spends practically all his time on the bedpan or in the toilet, who has no future whatever, and are able to aid him to become a useful citizen, our efforts are well worth while. The weight of such patient, a youth of 18 with long-standing colitis, 6 feet tall and weighing 80 pounds, after an ileostomy increased to 165 pounds. After complete resection of the colon he found employment and is helping to support his family.

DR. WILLIAM C. BOECK, Los Angeles: The view held before 1925 was that this disease should be treated primarily by surgery. Then in 1925, after the work of Bergen, we were led to believe that this disease could be treated by medicine. In the last thirteen years, as a result of the investigations of Bergen and others, I have come to four definite conclusions: 1. There is now an accepted clinical, roentgenologic and pathologic description of this disease which heretofore was quite unknown and was confused with tuberculosis and other conditions. 2. We are still in the dark as to the etiology. 3. This disease is known to be of a chronic relapsing type and it may go on for many years even though nothing is done for the patient. 4. There is a hopeless prognosis in many of the fulminating cases. It is generally agreed that the treatment is primarily medical to begin with. Furthermore, medical treatment is nonspecific and unsatisfactory. Probably medical cures are not brought about, but only an arresting of the disease. It may recur at any time. This was emphasized by Dr. Mackie. The surgeon, however, does bring about a cure when he performs a total colectomy, and that is the only "cure" I know of. Because of the unsatisfactory medical treatment there is again a trend toward surgery, and we have heard a plea today for colostomy, especially for those conditions which are limited to the rectum or the sigmoid-rectum portion of the colon. The only criticism that I would have for this procedure is

that in many cases the condition will remain limited to this area of the colon for years and never go any higher and such people cannot be induced to have a colostomy. Furthermore, I have had cases in which transverse colostomy has been done and the infection did not remain limited to the rectum but not only progressed to the ascending colon but also involved the stoma and even the skin of these patients. There isn't any assurance that just because one is going to do transverse colostomy one will limit it to the left side of the colon. It can go beyond that and has done so. A surgeon deserves a great deal of credit if he wants to operate on these patients. There is no other field of elective surgery with such a great mortality, even in neurosurgery. I think we should get together and spend some money on investigation to see whether we can't combine the medical and surgical treatment and obtain a better solution than exists at present.

DR. ARTHUR L. BLOOMFIELD, San Francisco: Surveying the whole field, none of us seem to be very happy about ulcerative colitis. You remember the despairing cry of the physician in Macbeth: "This disease passeth our art." I am afraid that is the situation with ulcerative colitis. We are mostly sail and very little anchor. It does seem to me of interest to line up ulcerative colitis with certain other "itises" which seem in many ways to be somewhat analogous. There is this very interesting group of chronic, semi-inflammatory, semidegenerative diseases the etiology of which is not clear. I might mention iritis, choroiditis, arthritis, hepatitis, along with ulcerative colitis. They all occur in very acute form and the patient may promptly get well and remain well, or they may begin in acute form and go ahead with a fulminating course, or there may be slower forms with relapses, finally passing into a chronic state. In all these diseases the etiology is unclear and, in all, attempts have been made to incriminate bacteria of one sort or another, usually with little success. It has been brought out that no specific etiologic agent has been proved. The most useful advance in recent years is the delivery of the patient with ulcerative colitis from the tortures which he used to have at the hands of physicians; namely, the defective diets which produced deficiency disease and the local, corrosive irrigations of the colon, which most physicians have pretty much abandoned. I should like to say one word to reinforce what Dr. Cheney said about concentrated liver extract. I am extremely cautious about therapy and still I have been immensely impressed by this series of cases. One of these patients is a young man who has been through the whole gamut of treatment, including sulfanilamide, with which, incidentally, I have had very poor results, fever therapy, vaccines, serums and high vitamin diets. At Dr. Cheney's suggestion I treated him with concentrated liver extract, and the result was remarkable. Of course, it is too soon to say whether he will be cured.

DR. JULIAN M. RUFFIN, Durham, N. C.: There are certain aspects of Dr. Mackie's paper which I wish to discuss. In my experience there has been no one organism which is constantly present. In a group of fifty patients the most frequent organisms were hemolytic *Endamoeba coli* and streptococci. Bagen's bacillus is inconstantly present, and I have been unable to grow a dysentery bacillus in a single case. Agglutinations were likewise negative. I feel, therefore, that there is no one organism which is responsible for the disease. Dr. Mackie has properly emphasized the importance of food sensitivity and certainly in some cases this does occur. I recall two cases in which a fulminating relapse immediately followed the ingestion of raw peanuts. The relationship of ulcerative colitis to a deficiency state is unquestionably true but I do not believe that ulcerative colitis can be regarded as a primary deficiency in the same sense as pellagra. A comparison of the proctoscopic appearance of the patients with ulcerative colitis with that of pellagra is of interest. In patients with pellagra who have the dermatitis but no sore tongue and no diarrhea the rectal mucosa is entirely normal. If, however, the patient has a sore tongue and diarrhea, invariably the rectal mucosa will be found to be diffusely inflamed and hyperemic, but never have I observed ulcers or the granular appearance which is so characteristic of ulcerative colitis. The importance of liver therapy has been pointed

out and in my experience marked improvement has been observed in certain cases following the use of liver extract. Dr. Mackie has given a most intelligent and comprehensive outline for the handling of the medical aspects of chronic ulcerative colitis.

DR. S. L. BERNSTEIN, Cleveland: I have no specific remedy for this disease but I want to make a slight contribution by telling of a result which I have had recently in a number of cases. I am impressed with what Dr. Cheney said about the use of liver, and in conjunction with that I have used enteric coated tablets of potassium permanganate 1 grain (0.065 Gm.) each.

DR. SIDNEY A. PORTIS, Chicago: I am sure that physicians are agreed that there is no specific etiologic factor at the present time producing ulcerative colitis. If there is no specific organism, it would seem logical that we should concern ourselves with those changes in the colon which predispose to secondary ulceration. What lowers the resistance of the colon that it should be the site of these lesions? Certainly bacillary dysentery may play a role. Bagen's organism may be found in a certain percentage of the cases. An interesting feature of this disease is that it practically always begins in the rectum and the sigmoid. Anatomically this is a fixed portion of the bowel. Therefore the trauma of hard, inspissated stools may irritate a sensitive colon and predispose to secondary ulceration. As Dr. Mackie has pointed out, this is one disease in which bismuth should not be used, because bismuth only helps to increase the consistency of the stool and make it more firm and in turn produces a pressure necrosis which promotes secondary ulceration. I have seen two cases at necropsy in which pressure ulceration from the use of bismuth has resulted. Further, I should like to call attention to the fact that the disturbances in metabolism and particularly mineral metabolism, with deficiency of chloride, may lower the resistance of the bowel wall and produce secondary ulceration. May not some of these cases, more or less, mirror the picture of an azotemia, and similarly may not an ulcerative colitis, associated with a uremic picture, reemphasize the fact that disturbances of nitrogen metabolism may be an additional factor? Just because a patient has an organic disease of the colon, associated with diarrhea, the psychogenic factors that may play a role in keeping up the gastrointestinal manifestations are frequently overlooked. Within the last year I have seen two cases of ulcerative colitis which did not improve under ordinary medical management, and with a psychoanalytic approach to their problem the diarrhea was almost completely ameliorated and there was a marked improvement in the clinical picture.

DR. JOSEPH FELSEN, Brooklyn: Based on experience in the East, chronic ulcerative colitis is nothing more than a late manifestation of bacillary dysentery. As the incidence of acute bacillary dysentery in this country, particularly during the past five years, is studied, one finds that the disease, according to actual figures available at the moment, has increased sixteen times. It appears to me, moreover, that the incidence of chronic ulcerative colitis has paralleled the increasing incidence of acute bacillary dysentery. Conclusive proof of this statement cannot be presented, however, until adequate follow-up studies of cases of acute bacillary dysentery are carried out, as were done in the Jersey City epidemic of 1934. Let me revert to some of the statements that have been made here this morning. I think it is very difficult to explain away twenty-one cases of chronic ulcerative colitis in which bacillary dysentery was definitely proved to be the etiologic agent. One cannot explain that away by any method of reasoning; moreover, in the other cases, let's say 80 per cent of them, the failure to obtain a positive culture does not necessarily mean that the original acute disease was not bacillary dysentery. In the acute form of the disease, the organism often disappears by the end of the tenth day. The serologic titer is no diagnostic criterion by itself. It is necessary to correlate all the various factors, epidemiologic, pathologic, serologic, clinical. As a result of such studies I feel more strongly than ever that chronic ulcerative colitis is nothing more than a late manifestation of bacillary dysentery. With regard to the surgical treatment, my experience coincides largely with that of many of the preceding speakers. The difficulties in surgery are chiefly these: Too much is expected of the

surgeon. If the surgeon will realize that the spread of intramural infection in the bowel from a segmental area of chronic ulcerative colitis is far beyond the reach of the naked eye and that no clue is afforded as to the extent of infection by the presence of mesenteric or mesocolic lymph nodes, he can readily understand why recurrences take place or why the patient dies of peritonitis. In New York, the cases I have been able to investigate have shown that the surgeon has cut through infected bowel or has overlooked a "skip" area, and the patient is no better after surgery than before. One cannot tell even in a postmortem specimen where the infection begins or ends.

Dr. A. H. AARON, Buffalo: The great majority of physicians have agreed that they do not know the cause of chronic nonspecific ulcerative colitis and that there are so many factors entering into the question that it is difficult without the most elaborate equipment to determine the etiologic factor in a very small group of those having the disease. One is left to try bacillary serum, then Barger's serum and vaccine, then all those agents that are going to be in the food factor group, and then the substances to solidify the stool. There is no intestinal antiseptic of any value; it has been agreed that the therapeutic enema has little value in the treatment of this condition. Rest is one of the most important factors. A diet can be arranged that will supply those factors which we honestly know something about, not a widespread vitamin administration of proprietary substances of whose exact action we know so little at the present time in this disease. I feel certain that when we hear of the excellent results of administration of liver in these cases we know we are dealing with the results of dietetic deficiencies due to prolonged ulcerative colitis. Please don't surfeit these patients with all these injections and therapy that we have been guilty of using. Remember that there is no factor in the cure of disease that equals rest and that we can establish a diet that will prevent them from acquiring deficiency states.

Dr. THOMAS T. MACKIE, New York: Emphasis has been placed on the therapeutic value of liver extract. I agree with Dr. Aaron that response to this preparation is indicative of failure to absorb or to utilize specific dietary factors which should be obtained from food. I have restricted liver therapy largely to patients presenting what I consider objective indications of deficiency disease. These comprise changes of the buccal and lingual mucosa similar to those seen in sprue, pellagra or pernicious anemia, and the gradual change from a microcytic to a macrocytic type of anemia. The caution that partial resection may be followed later by involvement of the remaining previously normal segment calls for reemphasis of the vital importance of complete study prior to resort to surgery. Such study may require months of observation to permit certain identification of contributory factors. These should constitute not only the basis of preoperative preparation but the basis of a permanent regimen for the patient after surgical intervention. For example, if successive addition and withdrawal of a particular food is accompanied by predictable exacerbation or quiescence of the inflammatory process, this food should be permanently forbidden. It is impossible to determine how far the colon may be sensitized or to predict the end result of continued exposure to the sensitizing agent. A recent experience with a case of the segmental type is illustrative. The entire colon proximal to mid-descending was extensively involved, the distal portion was normal. Preoperative dietary studies yielded clearcut evidence of sensitization to several foods, including milk and wheat. Following subtotal resection and ileosigmoidoscopy the allergic response was materially changed in character but not eliminated. Marked intestinal symptoms invariably follow the ingestion of foods previously found to disagree. A note of discouragement creeps into most discussions of the therapy of ulcerative colitis. Certainly this is justified with respect to achievement of complete cure by medical measures alone in many cases. On the other hand, many patients can be returned to a life of reasonable activity and of reasonable usefulness to the community and to themselves, granted adequate individualized study and cooperation. For the severe cases radical surgery must be considered. It is these cases particularly which require the most careful study prior to operation if operative mortality and follow-up results are to be satisfactory. The importance of the medical-surgical

team approach in both the preoperative and postoperative periods cannot be too strongly emphasized.

Dr. THOMAS E. JONES, Cleveland: With regard to Dr. Boeck's remarks about the jumping over of the infection, I tried to make it clear that if the colostomy is made properly it can obviate its occurrence. I have never seen a single case in which it has taken place. Maybe the organisms in Los Angeles are pretty high jumpers. Of course every surgeon will admit that the mortality is high. Why? Because patients have been carried on indefinitely under medical treatment and the only time the surgeon gets them is when they are practically moribund. We are not proud of that. We should like to obviate it but that is the reason for it—nothing else. It is just delay. Dr. Fitzgibbon has had an unsatisfactory experience with colostomy. Perhaps he has. I don't want him to have the misunderstanding that I jump right in and do it when the patient comes in. He is given a long period of rest and the operation is done in the quiescent stage, of course, and not as an emergency operation. I feel that Dr. Aaron has summarized this problem in a very sane manner. Put the patient to bed. Take two years, if necessary. Try allergy, vaccine, serum, diet, drugs, and if the patient has a recurrence, do a properly placed colostomy early rather than late.

Dr. J. F. PESSER, Trenton, N. J.: I should like to stress again the importance of continuous active treatment, utilizing every measure to maintain nutrition, and to improve the resistance to the highest possible level.

## THE INCIDENCE OF PRIMARY BRONCHIOGENIC CARCINOMA

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A review of the literature indicates that the incidence of primary bronchiogenic carcinoma has shown a definite increase in recent years. The increase has been shown to have occurred not only in the United States and Canada but in the various European countries as well, particularly Germany. Pässler in 1896 collected fifty-seven cases of cancer of the lung, as compared with Adler, who in a study made in 1912 was able to collect 360 cases from the literature. In his study Adler stated that failure to recognize this type of tumor had for a long time sustained the belief that it is a rare condition.

### INCIDENCE

Klotz<sup>1</sup> cited the literature showing the varying incidence of primary bronchiogenic carcinoma found by observers in succeeding periods. Thus Rheinhardt in 1878 noted cancer of the lung in 0.057 per cent of all autopsies; Fuchs in 1885 observed it in 0.065 per cent, Wolf in 1894 in 0.223 per cent, Oerstrom in 1907 in 0.31 per cent and Briese in 1916 in 0.46 per cent, and Barron in 1922 observed primary bronchiogenic carcinoma in 0.9 per cent of autopsies.

In recent years the incidence has risen at an accelerating rate. The continued rise, however, has not been noted equally in all localities, and there are reports from isolated clinics and hospitals where the incidence of primary cancer of the lung remains low. In 1934 Hill<sup>2</sup>

From the Medical and Hospital Service, Veterans Administration. Technical assistance in this study was rendered by E. K. Steet, A. Bamberg and Blanche B. Wilcox.  
Dr. Matz died June 25, 1938. At the time of his death he was chief of the Research Subdivision, Veterans Administration.  
Read before the Section on Pathology and Physiology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 17, 1938.  
1. Klotz, Oskar: Cancer of the Lung: with a Report upon Twenty-Four Cases, *Canad. M. A. J.* 17: 989-996 (Sept.) 1927.  
2. Hill, R. M.: Primary Cancer of the Lung: Its Incidence and Pathology, *Edinburgh M. J.* 41: 320-333 (May) 1934.

stated that cancers of the lung are seen in about 1 per cent of all autopsies and comprise more than 8 per cent of all malignant neoplasms discovered post mortem. In England the statistical data show a steady rise in the incidence of primary bronchiogenic carcinoma. Studies by German observers indicate that pulmonary neoplasms of this type have shown an increased incidence during the past few years, both those discovered ante mortem and those seen post mortem. The statistical data of other European countries also indicate an increasing incidence of this form of neoplasm. Simons<sup>3</sup> summarized the statistical proof of the increasing incidence of the disease in North America by tabulating the figures presented by eleven authors. The material included 22,754 necropsies and 669 carcinomas, of which 137 were pulmonary cancers. Cancers of the lung observed at autopsy increased from none in 1899 to 1.55 per cent in 1930. A similar increase in the ratio of cancers of the lung to all cancers was found; the percentage varied from 5.88 during the years 1910 to 1914 to 8.28 during the years 1925 to 1928.

#### INCIDENCE OF PRIMARY BRONCHIOGENIC CARCINOMA IN THE VETERANS' GROUP

The present study was initiated in order to ascertain whether or not additional knowledge could be derived from the statistical data of the Veterans Administration on the incidence of carcinoma in general and of bronchiogenic carcinoma in particular. It was thought that it might be possible to learn the effect of advancing age on the incidence of primary bronchiogenic carcinoma in a selected group of men of whom the largest number had reached the cancer age period.

The data in this study are based on autopsies performed in the hospitals of the Veterans Administration. Permission for autopsy is obtained in about 41 per cent of deaths of veterans in Veterans Administration hospitals; the percentage varies with the type of hospital, being highest in those primarily for patients suffering from medical and surgical disorders.

A study of table 1, showing the data from 1927 to the first six months of 1937 inclusive on the percentage relation of primary bronchiogenic carcinomas to all autopsies, indicates that the percentage varied from a low of 0.4 to a high of 5.3. It also varied from year to year; the highest percentage was found in the six month period of 1937. The figures for 1927 to 1937 indicate that the percentage relation of primary bronchiogenic carcinomas to all carcinomas varied from a low of 2.7 per cent to a high of 23.4 per cent. In 1928 no bronchiogenic carcinomas were observed at autopsy. The consolidated figures show that 13.7 per cent of all carcinomas were of the primary bronchiogenic type.

The total number of primary bronchiogenic carcinomas from 1927 to the first six months of 1937 inclusive was 160. All carcinomas found during this period numbered 1,167, and the autopsies performed, 7,398. In studying the figures it was found that there had been a steady rise in the number of all carcinomas, as well as in the bronchiogenic type, from 1931 to 1937.

#### NATURE OF INCREASED INCIDENCE

The literature on the nature and the causes of the increasing incidence of primary bronchiogenic carcinoma is extensive. Most of the studies have been made by European observers. However, a number of American clinicians and pathologists also have investigated

the various phases of this problem for the purpose of learning whether the increased incidence of this type of tumor is absolute or relative.

The observations of Rosahn<sup>4</sup> at the Boston City Hospital are most convincing as to the nature of the increased incidence. In the period 1925 to 1928 the percentage relation of all cancers to all autopsies at the Boston City Hospital increased by 20 per cent, while the percentage relation of primary carcinoma of the lung to total autopsies increased by 81 per cent and the percentage relation of primary carcinoma of the lung to all cancers showed an increase of 49 per cent. These figures indicate that the increase of the incidence of primary bronchiogenic carcinoma was much greater than the increase of the incidence of all cancers. The data are suggestive of an absolute increase of primary cancer of the lung. At the Mayo Clinic, Lemon, Vinson, Moersch and Kirklin<sup>5</sup> found a steadily increasing number of primary bronchiogenic carcinomas since 1925. There were almost three times as many positive diagnoses made of this form of cancer in 1931 as in 1927. These observers reached the conclusion that there has been an actual increase of this type of tumor.

Simons<sup>3</sup> expressed the opinion that the incidence of the disease has increased both absolutely and relatively; that continued suggestions that such an increase is only apparent are refuted by the facts; that the increase was gradual until the early 1900's, the gradient of increase having become constantly steeper since then, and, finally, that in many localities the greatest incidence seems to have been reached in 1924, while in others the frequency is still advancing.

In the foreign literature also the question whether the increased incidence of primary bronchiogenic carcinoma is absolute or relative shows a divergence of opinion. In Great Britain, Simpson,<sup>6</sup> after a study of his data and the data of others, concluded that the increased incidence of carcinoma of the lung is a real one and that it is not associated with a comparable increase of total carcinomas.

Hanf made a study of the incidence of primary bronchiogenic cancer in the Pathologic Institute of the University of Berlin. She noted that the increase was parallel with that of other cancers. Her conclusion was that the increase of primary bronchiogenic carcinoma is in all probability only apparent. Katz investigated all cases of primary cancer of the lungs in the autopsy records for sixty years at the Heidelberg Pathologic Institute. His table, showing the incidence of pulmonary cancers and of all cancers for the years 1906 to 1926, shows a relative as well as an absolute increase of bronchiogenic carcinoma.

#### FACTORS CAUSING INCREASED INCIDENCE

Since primary bronchiogenic carcinoma has shown an increased incidence in recent years, the question arises as to the factors which have been responsible. Many observers attribute the increase to the epidemic of influenza in 1918-1919. On the other hand, Kerley said that cancer of the lung has never been reported in Iceland, where the ravages of influenza have been exceptionally severe. Other authorities have said that the increase is due to industrial expansion, tarred roads,

4. Rosahn, Paul D.: The Incidence of Primary Carcinoma of the Lung, *Am. J. M. Sc.* 179: 803-810 (June) 1930.

5. Lemon, Willis S.; Vinson, Porter P.; Moersch, Herman J., and Kirklin, B. R.: Primary Carcinoma of the Bronchus, *Southwestern Med.* 16: 485-493 (Dec.) 1932.

6. Simpson, Samuel Levy: Primary Carcinoma of the Lung, *Quart. J. Med.* 22: 413-449 (April) 1929.

3. Simons, Edwin J.: Primary Carcinoma of the Lung, Chicago, The Year Book Publishers, Inc., 1937.

increased longevity, improvement of diagnostic methods and a number of other factors.

Hamman<sup>7</sup> referred to the factors cited by other authors as being responsible for the increased incidence of cancer of the lung and concluded that there has been an actual increase of the incidence of this type of neoplasm. Kennaway and Kennaway, in a study of

TABLE 1.—Incidence of Primary Bronchiogenic Carcinoma in Patients of the Veterans Administration

Year	Autopsies	Carci- nomas	Carci- nomas to Autopsies, Per- centage	Broncho- genic Carci- nomas	Primary Broncho- genic Car- cinomas to All Autopsies, Per- centage	Primary Broncho- genic Carci- nomas to All Car- cinomas, Per- centage
1927	106	12	6.1	2	1.0	16.7
1928	378	26	6.9	0	0.0	0.0
1929	402	51	10.3	0	1.8	17.6
1930	632	66	10.4	3	0.5	4.5
1931	775	110	14.2	3	0.4	2.7
1932	827	145	17.5	20	2.4	13.5
1933	837	144	17.2	21	2.5	14.6
1934	1,010	161	15.9	18	1.8	11.2
1935	910	166	18.2	20	2.9	15.7
1936	920	192	20.9	30	3.9	18.7
1937*	419*	91*	22.4	22*	5.3	23.1
Total	7,395	1,167	15.8	160	2.2	12.7

\* First six months.

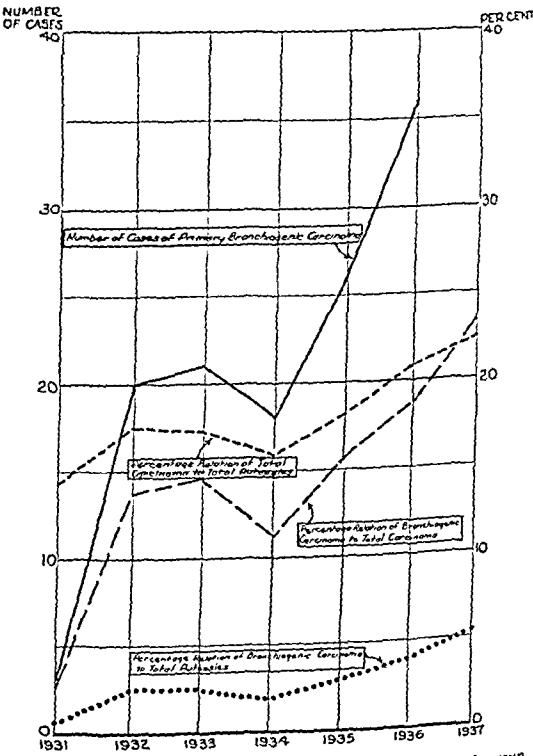
a large number of death certificates, found that certain classes of laborers are especially liable to cancer of the lung. Among these are road workers, metal grinders, employees in gas works and persons engaged in the tobacco trade. Arkin and Wagner<sup>8</sup> stated that twenty years ago only 5 per cent of primary bronchiogenic carcinomas were diagnosed clinically, while today about 50 per cent are recognized during life. This would appear to show that better diagnostic methods have contributed to the increase in the number that are recognized and the consequent increase of the incidence of this type of tumor.

This brings me to the consideration of the data in table 1 on the nature of the increased incidence of carcinoma in general and of primary bronchiogenic carcinoma in particular in the veterans' group. The percentage relation of all carcinomas to all autopsies was 17.5 per cent in 1932 and 22.4 per cent in 1937, an increase of 28 per cent. The percentage relation of primary bronchiogenic carcinomas to all autopsies varied from 2.4 per cent in 1932 to 5.3 per cent in 1937, an increase of 120.8 per cent. Finally, the percentage relation of primary bronchiogenic carcinomas to all carcinomas varied from 13.8 per cent in 1932 to 23.4 per cent in 1937, an increase of 69.6 per cent.

The statistical data representing the relation of primary bronchiogenic carcinomas to all carcinomas are of importance, as they indicate the nature of the increased incidence. If the increased incidence were dependent on and due to an increase of all carcinomas, the percentage relation each year would be about the same and would be constant over a period of years. A graph showing the relation would be represented by a horizontal line. But, as seen in chart 1, the trend is definitely upward. It may therefore be concluded that the increased incidence of primary bronchiogenic carcinoma is absolute.

In order to confirm further the observation that the increase of primary bronchiogenic carcinoma is absolute, a study was made of the yearly incidence of cancer of two other inaccessible sites, the colon and prostate, from 1931 through the first half of 1937, and of the percentage relation of each of these two types of cancer to all carcinomas during the same period. It was found that there was little annual variation in the incidence of these two types of carcinoma and their relation to the total number of carcinomas. In other words, the incidence from year to year was fairly constant and related to the incidence of all carcinomas, as compared with the incidence of bronchiogenic carcinoma, which was not so dependent and the increase of which was considered absolute.

In addition to an absolute increase, an analysis of the data shows that there is also a relative increase of primary bronchiogenic carcinoma. In other words, the relative increase of this type of tumor in the veterans' population is dependent on a number of factors. One of these factors is the expansion of the facilities for the diagnosis and treatment of cancer in the Veterans Administration since 1930; the administrator authorized the establishment at that time of the Tumor Clinic at Hines, Ill., and subsequently of a number of such clinics in other cities. Thereafter the interest in cancer was accentuated, and the number of bronchiogenic carcinomas diagnosed ante mortem increased. In



Incidence of primary bronchiogenic carcinoma in veterans' group.

addition, when a pulmonary condition was suspected of being primary bronchiogenic carcinoma but was not diagnosed ante mortem, autopsy was performed and the condition then recognized; accordingly there was an increase in the number of carcinomas found at autopsy.

Still another cause of the relative increase of primary bronchiogenic carcinoma is the age distribution of the veterans' group. It is noted that from 1930 to 1937 the average age of all veterans was from 40 to 47. This

7. Hamman, Louis: The Diagnosis of Carcinoma of the Lung, Am. Rev. Tuberc. 28:711-733 (Dec.) 1933.  
8. Arkin, Aaron, and Wagner, David H.: Primary Cancer of the Lung, J. A. M. A. 106:587-591 (Feb. 22) 1936.

period included the ages at which the largest number of primary bronchiogenic carcinomas was found. Thus in 118, or 85 per cent, of 138 cases in which a record is available as to the year of onset, there was evidence of onset between 1931 and 1936. Accordingly the increase of primary bronchiogenic carcinoma during the past few years has in part been due to the aging of the veterans.

DISEASES OF THE RESPIRATORY TRACT AS CAUSATIVE FACTORS IN CANCER OF THE LUNG

In 1920 Winternitz actually prophesied that an increase of primary bronchiogenic carcinoma would follow the influenza epidemic, because he found that influenza and influenza-pneumonia frequently resulted in metaplasia of the bronchial epithelium and a proliferation of the young cells to the extent that it was difficult to distinguish the cellular condition micro-

atypical cell regeneration, metaplasia and cell nest formation, indicating a tendency for this disease to cause irregularities of cell growth.

In this connection I wish to quote the opinion of Wells,<sup>11</sup> who maintained that if the increased incidence of cancer of the lung is a sequel of influenza, the increase should be transitory, but that if it is the result of industrial expansion and irritation of the respiratory tract by noxious chemicals and gases, or if it is due to dust from tarred roads, the increase may become permanent and significant.

The relation of pulmonary tuberculosis to the inception of cancer has also been the subject of considerable discussion among observers. Ewing is an exponent of the view that pulmonary tuberculosis is a factor in the causation of primary bronchiogenic carcinoma. Davidson<sup>10</sup> stated that the association of cancer of the lung and tuberculosis is a question which has given

TABLE 2.—Relation of Preceding Disease of the Respiratory Tract to Primary Bronchiogenic Carcinoma

	Influenza	Bronchitis	Pneumonia	Pleurisy	Pulmonary Tuberculosis	Bronchial Asthma	Residuals of Warfare Gassing
Total number of instances of preexisting disease of the respiratory tract...	28 29.3%	27 19.6%	21 15.2%	29 21.0%	13 9.4%	11 8.0%	7 5.1%
	10	6	8	10	6	2	0
Bronchitis.....	1	1	4	4	..	..	..
Pneumonia.....	1	..	1	3	1	1	2
Pleurisy.....	4	3	1	..	3	1	1
Pulmonary tuberculosis.....	..	1	..	3	..	1	..
Bronchial asthma.....	..	1	1	1	1	..	..
Residuals of warfare gassing.....	..	2	1	..	..	..	..
Influenza and bronchitis.....	..	..	1	2	1	3	..
Influenza and pneumonia.....	..	1	..	1	..	..	..
Influenza and pleurisy.....	..	2	1	..	..	..	..
Influenza and pulmonary tuberculosis.....	..	1	..	..	..	..	..
Influenza and asthma.....	..	3	..	..	..	..	..
Bronchitis and pleurisy.....	2	..	..	..	1	..	1
Bronchitis and pulmonary tuberculosis.....	1	..	..	1	..	..	..
Bronchitis and bronchial asthma.....	3	..	..	..	..	..	..
Bronchitis and residuals of warfare gassing.....	..	..	1	1	..	..	..
Pneumonia and bronchitis.....	1	..	..	..	..	..	1
Pneumonia and pleurisy.....	1	..	..	..	..	..	..
Pneumonia and residuals of warfare gassing.....	..	1	..	..	..	1	1
Tuberculosis and pleurisy.....	..	1	..	..	..	..	..
Pleurisy and residuals of warfare gassing.....	..	1	..	..	..	..	..
Bronchial asthma and residuals of warfare gassing.....	..	..	1	..	..	..	..
Influenza, pleurisy and bronchitis.....	..	..	..	..	..	..	1
Influenza, bronchitis and residuals of warfare gassing.....	..	..	..	1	..	..	..
Influenza, pleurisy and residuals of warfare gassing.....	..	1	..	..	..	..	..
Bronchitis, pleurisy and bronchial asthma.....	..	..	1	..	..	..	..
Bronchitis, pleurisy and residuals of warfare gassing.....	1	..	..	..	..	..	..
Pneumonia, bronchitis and bronchial asthma.....	..	..	..	1	..	..	..
Pneumonia, pleurisy and bronchitis.....	..	..	..	..	..	1	..
Pneumonia, pleurisy and bronchial asthma.....	..	1	..	..	..	..	..

scopically from neoplasm. The studies of Barron, Fried and Moise showed an increase of cancer of the lung dating from the influenza epidemic.

On the European continent data on the relation of influenza to cancer of the lung are conflicting and are not as clear cut as those shown by the American investigators. The observations of Duguid<sup>9</sup> in Great Britain show a somewhat irregular increase but do not suggest an obvious relation of cancer of the lung to the influenza epidemic of 1918. However, the postmortem statistics of the London Hospital indicate an increase of cancer of the lung.

Shuster, as quoted by Davidson,<sup>10</sup> submitted the following arguments in favor of the idea that influenza is a predisposing cause of pulmonary carcinoma: (1) the coincidence of epidemics of influenza and the increase of lung cancer; (2) the special tendency in influenza for chronic inflammation to persist, with pulmonary fibrosis and bronchiectasis, and the fact that these processes occur in cancer of the lung in varying degrees, and (3) the observation in lungs affected by influenza of

rise to a certain amount of discussion. In a study of the Brompton Hospital series of 107 cases in which autopsy was performed, only seven persons, or 6.5 per cent, were found to have definite evidence of tuberculous disease and primary bronchiogenic carcinoma.

Other diseases of the respiratory tract are mentioned by various observers as preceding the onset of cancer of the lung and as being factors in the causation of this type of tumor.

In analyzing the available data in the literature with regard to the relation of preceding disease of the respiratory tract to primary bronchiogenic carcinoma, I may state that there is a suggestion that certain pulmonary diseases have in recent years appeared more frequently and that, as a result of their irritating influence on the bronchial mucosa, cancer of the lung has developed in susceptible persons.

In an effort to learn whether or not certain preceding diseases of the respiratory tract were factors in the inception of primary bronchiogenic carcinoma in the veterans' group of 138 cases, a study was made of the clinical records in these cases, including a review of

9. Duguid, J. B.: The Incidence of Intrathoracic Tumours in Manchester. *Lancet* 2:111-116 (July 16) 1927.  
10. Davidson, Maurice: Cancer of the Lung and Other Intrathoracic Tumours, London, John Wright & Sons, Ltd., 1930.

11. Wells, H. Gideon: Cancer Statistics as They Appear to a Pathologist. *J. A. M. A.* 88: 476-482 (Feb. 12) 1927.



the medical history previous to the patient's admission to military service. This study revealed that eighty-one, or 58.7 per cent, of the men gave evidence of one or more preceding diseases of the respiratory tract which caused irritation of the bronchial mucosa, with a possible proliferation of the lining cells and resulting metaplasia. The diseases which were most frequently reported were influenza, bronchitis, pneumonia, pleurisy, pulmonary tuberculosis, bronchial asthma and the residuals of warfare gassing. These conditions existed alone or in various combinations; the number and percentage of cases of each disease in the 138 cases may be found in table 2.

It is believed that the incidence of preceding diseases of the respiratory tract in this group of cases is sufficiently great to be suggestive that such conditions constituted one factor which may have led to the inception of primary bronchiogenic carcinoma. It is realized, of course, that other causative factors are involved, such as heredity, individual predisposition and perhaps tissue or organ susceptibility; but these factors may be

fourth, were from 30 to 39, and twenty-six, or approximately 19 per cent, were from 50 to 59. The youngest was 21 and the oldest 74 at the time of the inception of the tumor; the average age at the time of onset was 45.

An analysis of these data shows that the veterans give evidence of a younger age incidence for the onset of primary bronchiogenic carcinoma than is noted in civil life. This is due to the fact that with them one is dealing with a group of men, of whom the largest number are in the younger age groups. These data would seem to indicate that one may expect to see a larger number of patients with primary bronchiogenic carcinoma in the veterans' group in the immediate future.

#### OCCUPATION

The question whether certain occupations are a factor in the inception of primary bronchiogenic carcinoma is controversial. Rosedale and McKay,<sup>12</sup> in a study of fifty-seven cases of primary bronchiogenic carcinoma, found that in forty-three, or 75.4 per cent, the patient

TABLE 3.—Age Incidence of Bronchiogenic Carcinoma

Age Group, Years	Rogers		Hill		Olson		Arkin and Wagner		Harvey		Frissell and Knox		Simpson		Brines and Kenning		Total	
	Num- ber	Per- cent- age	Num- ber	Per- cent- age	Num- ber	Per- cent- age	Num- ber	Per- cent- age	Num- ber	Per- cent- age	Num- ber	Per- cent- age	Num- ber	Per- cent- age	Num- ber	Per- cent- age	Num- ber	Per- cent- age
Unrecorded....	...	...	22	2.2	...	...	...	...	...	...	...	...	...	...	...	...	22	1.2
10-20.....	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	5	0.3
20-29.....	...	...	63	6.6	12	4.1	3	2.2	4	4.0	3	6.5	6	4.3	1	1.5	94	5.2
30-39.....	2	4.0	139	14.2	25	8.5	9	6.7	14	14.0	5	10.9	18	12.9	10	14.7	222	12.2
40-49.....	7	14.0	257	26.2	53	17.9	39	28.9	23	23.0	6	13.0	41	29.5	18	26.5	444	24.5
50-59.....	24	48.0	300	30.6	105	35.6	59	43.7	32	32.0	17	37.0	45	32.4	27	39.7	609	33.6
60-69.....	12	24.0	198	20.2	60	20.3	22	16.3	19	19.0	14	30.4	21	15.1	10	14.7	356	19.6
70-79.....	5	10.0	...	...	30	10.2	3	2.2	8	8.0	...	...	4	2.9	2	2.9	52	2.8
80 and over....	...	...	...	...	10	3.4	...	...	...	...	...	...	...	...	...	...	10	0.6
Total.....	50		981		295		135		100		46		139		68		1,814	
Average.....	50.7		51.0		53.7		...		...		...		4.8		...		...	
Youngest.....	37		...		29		...		21		17		13		...		...	
Oldest.....	77		...		89		...		...		69		77		...		...	

regarded as predisposing in comparison with the diseases of the respiratory tract, which may be considered exciting factors. Suffice it to say that when these factors become operative at the cancer age primary bronchiogenic carcinoma was a result.

#### AGE INCIDENCE

Age is one of the factors concerned with the onset of primary bronchiogenic carcinoma. Its part in the development of this type of neoplasm is similar to its role in connection with carcinoma in general. There evidently is a certain period of life which is characterized by abnormal processes of one kind or another, predisposing to the onset of cancer; at this period a precipitating or exciting factor may conduce to the actual development of the neoplasm.

Considerable work has been done on the age incidence of primary bronchiogenic carcinoma. The data of a number of observers have been compiled and have been consolidated in table 3. These data show that of a total of 1,814 primary bronchiogenic carcinomas, the largest number had their onset in the age period 50 to 59, the second largest number in the age period 40 to 49 and the third largest number in the age period 60 to 69. As far as can be learned from the statistics the youngest patient was 13 and the oldest 89 at the time of onset.

In table 4, which gives the age at the time of onset of primary bronchiogenic carcinoma of 138 veterans, it is shown that sixty-seven, or almost one half, of the veterans were from 40 to 49; thirty-five, or one

was employed in an occupation requiring exposure to dust or other irritating atmospheric factors. The authors said that such exposure may be a factor in producing chronic irritation of the bronchial epithelium resulting in protoplasia and metaplasia. Simons<sup>3</sup> stated that until further information is obtained on the rela-

TABLE 4.—Age at Time of Inception of Primary Bronchiogenic Carcinoma in Veterans' Group

Age Group	Number of Cases	Percentage
20-29.....	2	1.4
30-39.....	35	25.4
40-49.....	67	48.6
50-59.....	26	18.8
60-69.....	7	5.1
70 and over.....	1	0.7
Total.....	138	100.0

Range, from 21 to 74 years  
Average age at time of inception, 45 years

tion of occupation to the inception of cancer of the lung, industrial hazards cannot be accorded any etiologic significance except as they involve chronic irritation of the lungs.

In this study, it was found that fifty, or 36 per cent, of the 138 patients gave a history of being connected with occupations or industries in which there was a

12. Rosedale, Raymond S., and McKay, Donald R.: A Study of 57 Cases of Bronchiogenic Carcinoma, *Am. J. Cancer* 26: 493-506 (March) 1936.

possibility of irritation and traumatization of the respiratory tract. The fact that so large a percentage had been engaged in occupations which caused them to be exposed to chronic irritation of the respiratory tract is suggestive that such occupations may have played a causative part in the inception of the primary bronchiogenic carcinoma.

#### HEREDITY

Whether or not heredity is a factor in the inception of primary bronchiogenic carcinoma is still questionable. Members of certain families do show a predisposition to cancer. On the other hand, cancer is such a widespread disease that one would expect to find it in some generations of many families. One might therefore be inclined to the view that it is hereditary in origin. A study of the clinical records of 138 cases showed that in twenty-one, or 15.2 per cent, there was evidence of a hereditary, familial or combined hereditary and familial history of cancer.

Hospital histories are frequently lacking in data on the hereditary or familial aspects of the disease involved. Accordingly it is not believed that the information on heredity noted in the histories in these cases is complete or does justice to this phase of the subject, so that no definite conclusion may be reached from the available information.

#### COMMENT

It has been the observation of physicians of the Veterans Administration that the incidence of primary bronchiogenic carcinoma in the veterans' group has been increasing at an accelerating rate during the past few years. The question has been asked What factors are responsible for the increase?

In order to obtain information which would throw light on this problem it was decided to make a study of the autopsy material of the Veterans Administration. Accordingly a careful review was made of 7,398 post-mortem protocols. These reports were based on autopsies performed between 1927 and the first half of 1937. A total of 160 records of bronchiogenic carcinoma were found in this material, of which 138, with the accompanying clinical records, were studied intensively.

This study revealed the fact that a definite increase of the incidence of carcinoma in general and of primary bronchiogenic carcinoma in particular has taken place. The percentage relation of all carcinomas to all autopsies increased by 28 per cent from 1932 to 1937; for the same period the percentage relation of primary bronchiogenic carcinomas to all autopsies increased by 120.8 per cent and the percentage relation of primary bronchiogenic carcinomas to all carcinomas by 69.6 per cent.

Of the increases just mentioned, that pertaining to the relation of primary bronchiogenic carcinomas to all carcinomas is important, as from a statistical standpoint it definitely shows that the increase is absolute. If the increased incidence of bronchiogenic carcinomas were related to and dependent on an increase of all carcinomas, the percentage relation each year would be about the same and would be constant over a period of years. A graph showing the relation would be represented by a horizontal line, whereas the actual graph shows a definitely upward trend. The statistical inference therefore is that the increased incidence of primary bronchiogenic carcinoma is absolute.

In order to find further support for the observation that the increase of primary bronchiogenic carcinoma is absolute, a comparative study was made of the annual

incidence of carcinoma of the colon and of the prostate and their percentage relationships to all carcinomas from 1931 to the first half of 1937. For this purpose these two types of carcinoma may be considered inaccessible and may be placed in the category with primary bronchiogenic carcinoma.

It was found that the incidence of these two tumors and their relation to all carcinomas were comparatively constant from year to year. This indicates that the incidence of carcinoma of the colon and of the prostate was related to the incidence of all carcinomas, as compared with the incidence of cancer of the lung, which was partly so related and was increasing. Accordingly, these data lend weight to the observation that the increase of primary bronchiogenic carcinoma is in part absolute.

When the increase of the incidence of primary bronchiogenic carcinoma in the veterans' group was found to be absolute, the question arose as to what factors were responsible. Accordingly attention was focused on preceding diseases of the respiratory tract, the reports of a number of observers who had made a study of this problem being kept in mind. It was found that in eighty-one, or 58.7 per cent, of the 138 cases there was evidence that acute or chronic diseases of the respiratory tract of various kinds, either singly or in combination, had been present prior to the inception of the neoplasm. The presence of chronic diseases of the respiratory tract in so large a percentage of these cases was suggestive that they played a part in the inception of the tumor in persons with predisposing heredity and age and increased tissue susceptibility.

Further study of the problem revealed that 36 per cent of the patients had been engaged in occupations which were accompanied by exposure to irritation of the respiratory tract and traumatization of various kinds. It was thought that such exposure may have had a part in the inception of the tumor in the veterans' group.

In a study of the statistical data in the 138 cases it was found that there was a steady rise in the number of carcinomas of all kinds as well as in the number of bronchiogenic carcinomas from 1931 to 1937. This rise coincided with the increase of the average age, which was 41 in 1931 and about 47 in 1937; in other words the rise began when many of the veterans entered the cancer age period and has continued since then. Accordingly the factors which have their fruition at or during the cancer age period and which contribute to the inception of malignant neoplasm have been playing a similar part in the cases under consideration and have been responsible for the relative increase of the incidence of primary cancer of the lung.

Finally, it was noted that the increase of the number of bronchiogenic carcinomas received impetus after the expansion of the facilities of the Veterans Administration for the diagnosis and treatment of cancer in 1930. It is believed that the establishment of the Cancer Clinic at Hines, Ill., and of the auxiliary clinics in other sections of the country stimulated interest in the diagnosis and postmortem study of primary bronchiogenic carcinomas, with resulting increased recognition of the existence of the tumor of the lung. This increased recognition may be cited as a factor responsible for the increased relative incidence of cancer of the lung in the veterans' group.

The factors which have been described as contributing to the absolute and relative increase of primary

bronchiogenic carcinoma in the veterans' group may be said to play similar parts in the increase of cancer of the lung which has been noted in recent years in the civilian population.

#### CONCLUSIONS

1. The incidence of primary bronchiogenic carcinoma in the veterans' population has been increasing during the past few years. This increase is both absolute and relative.

2. The absolute increase of this type of tumor is unrelated to the increase of carcinoma in general. The factors which may be responsible for the absolute increase of cancer of the lung are the large percentage of preceding diseases of the respiratory tract and the fact that a comparatively large number of the persons in this group were in occupations which were accompanied by exposure to irritations of the respiratory tract and traumatizations of various kinds.

3. One of the factors causing a relative increased incidence of bronchiogenic carcinoma is the added interest in cancer on the part of the physicians of the Veterans Administration, resulting in an increase of the number of cancers of the lung diagnosed ante mortem. In many of the cases in which carcinoma was suspected but was not definitely diagnosed ante mortem, postmortem examination was made; hence the increased incidence of this type of tumor in autopsy statistics.

4. Another factor which may be held responsible for the relative increase in the incidence of cancer of the lung is the entrance of the veterans' group into the cancer age period.

5. A comparative study of the data on the incidence of cancers of the lung according to age in the civilian population and in the veterans' group shows that the largest number of civilian patients are older than the veterans. One may therefore expect that as the veterans grow older an increasing number of primary bronchiogenic carcinomas will be seen among them.

#### ABSTRACT OF DISCUSSION

DR. MAX CUTLER, Chicago: The conclusions which Dr. Matz has drawn are in agreement with the opinions generally expressed by other students of the subject. There can be little doubt that the increase in the incidence of pulmonary cancer is not apparent but real. This fact raises implications concerning the etiology of bronchiogenic carcinoma which are interesting and possibly important. The increase in the frequency of cancer of the lung during the last few decades appears in all statistics including those from America, England, Germany, Austria and Switzerland. It is interesting to note that the increase in the frequency of this disease was not observed in all places at the same time. In Riga, for example, an increased incidence was noted as early as 1900 (Hanteln) and reached its peak in 1916 (Brandt). In Oslo and Innsbruck, on the other hand, a marked increased incidence has not been observed even in recent years. In Berlin, Hamburg and Basel a slightly increased incidence was noted in 1900 but did not become pronounced until recently, whereas in Basel the peak was reached in 1914 and no further increase has been observed since. In considering the possible causes for the increased incidence of cancer of the lung several questions arise, among which hereditary predisposition at once requires serious attention. The experiments of Maud Slye indicate that certain strains of mice are more prone to development of cancer of the lung than others, and Clara Lynch was able to produce cancer of the lung more rapidly and more frequently by application of tar in certain inbred strains than in other strains. Those experiments seem to indicate that the development of cancer of the lung after painting of the skin with tar is independent of the development of cancer in this area. Thus a special predisposition of the lung to the development of carcinoma under these con-

ditions is suggested. The etiologic relationship between certain irritating agents and cancer of the lung was demonstrated dramatically in the Schneeberg cancers which developed among miners in Saxony. A combination of arsenic and radium emanation contained in the dust proved to be the causative factors. In connection with the possible relationship of influenza to cancer of the lung, it is interesting to note that spontaneous occurrence of lung tumors among rats, which are also prone to other infectious lung diseases, were not observed. The evidence which has accumulated on this subject renders it difficult to escape the suspicion, if not the conclusion, that certain cell stimulating agents—infections and chemicals—probably play an important role in the etiology of cancer of the lung and that the increase in the incidence of this disease may possibly be related to some of these factors.

DR. PHILIP B. MATZ, Washington, D. C.: There is nothing I wish to add except to repeat that about 15.2 per cent of the group studied gave evidence of a hereditary or familial history of cancer. Although this figure seems high it should be considered the minimum for the group, as it is often difficult to obtain the familial and hereditary data from the clinical histories.

### SUBPIAL RESECTION OF THE CORTEX FOR FOCAL EPILEPSY

#### FURTHER OBSERVATIONS

LEONARD T. FURLOW, M.D.

ST. LOUIS

In 1909 Horsley<sup>1</sup> described a method of excision of an area of motor cortex for the relief of violent athetoid and convulsive movements of an upper extremity. This consisted in splitting the pia lengthwise over the center of the convolution to be partially excised, gradually pushing the pia back to the extreme edge of the sulcus on either side, and then removing the necessary amount of the convolution. In 1935 Sachs<sup>2</sup> reported experiences with this subpial resection of the cortex in the treatment of focal epilepsy and athetosis. The actual procedure he called the Horsley operation. Since that time there have been other cases in which it was thought that the procedure was indicated and, having found it to be of definite value, I am making this report.

In the paper<sup>2</sup> mentioned, eleven cases in which this operation had been done were reported. Two of the patients suffered from athetosis, five had a definite history of preceding severe trauma to the head, and in three the cortex was normal both grossly and microscopically. In the final case the convolution in which the motor arm center was located looked broader than normal and on microscopic study showed some gliosis, but no tumor. In three of the cases in which there was a history of preceding trauma the actual starting point of the convulsion, as determined by galvanic stimulation, was apparently not involved by any scar or adhesions, so that an accurate subpial resection could be carried out.

Up until the time of that report<sup>2</sup> and since, my associates and I have attempted to select and classify carefully all cases of focal epilepsy coming under our care. Observation over a number of days, if necessary, is carried out, and every effort is made to have one or

From the neurosurgical service of the Washington University School of Medicine and the Barnes and St. Louis Children's hospitals. Read before the Section on Nervous and Mental Diseases at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 17, 1938.

1. Horsley, Victor: The Function of the So-Called Motor Area of the Brain, *Linnacre Lecture*, Brit. M. J. 2: 125, 1909.

2. Sachs, Ernest: The Subpial Resection of the Cortex in the Treatment of Jacksonian Epilepsy (Horsley Operation) with Observations on Areas 4 and 6, Brain 58: 492 (part 4) 1935.

more convulsions observed by either a member of the staff or an experienced nurse, to verify the statement of the patient or the family that the seizures are focal. Exhaustive studies are made to determine or rule out the presence of a cerebral tumor, and naturally all cases of tumor have been excluded from this study. A careful evaluation of the patient's mental status is made, for it is our feeling that nothing can be accomplished by operations on patients who have extensive cortical degeneration. The post-traumatic cases are divided into two groups, those in which so widespread a trauma has occurred that a massive excision of a cortical scar is necessary, and those in which a more focal injury has occurred with a smaller area of scar. In the latter group of cases, if it is at all possible, we prefer to do a subpial resection rather than a removal of the scar with the electric knife.

The actual technical procedure is not difficult. Unless the patient absolutely refuses, the operation is done under local anesthesia for, with general anesthesia, much more electric current is required for cortical stimulation. After the dural flap has been reflected, careful examination of the exposed cortex is made. If nothing abnormal is found, stimulation with a unipolar galvanic electrode is done. The amount of current used is the minimal amount necessary to produce a slight contraction of the exposed temporal muscle, and, using this current we carefully and unhurriedly define the area of exposed cortex which when stimulated will reproduce the focal convulsive movements or sensory seizure. Then a nick is made in the pia in the center of the convolution, a small dural elevator is inserted beneath the pia (fig. 1), and it is incised with a pointed knife. Then with cotton pledgets the pia is gently rolled back to the edges of the sulcus (fig. 2), and with a brain spoon the necessary amount of convolution is removed (fig. 3), care being taken to stay inside the pia. There is no bleeding, and the area originally outlined is removed with exactness. It should be emphasized that the removal must include all areas which, when stimulated, produce the movement or sensation sought, for in several of the early cases it was necessary to do a secondary operation and remove more cortex because the original removal had not been extensive enough.

We now have sixteen cases in which this procedure has been carried out. Eleven of the patients had focal epilepsy with motor phenomena, three had attacks which combined motor and sensory phenomena, and two had violent athetotic arm movements.

The immediate postoperative course is interesting in view of the recent discussions as to the function of the so-called motor and premotor cortex. All areas of removed cortex have been studied by Dr. O'Leary of the Department of Cytology of the Washington University School of Medicine, and in every instance in which we have removed area 4 a spastic paralysis has occurred. We have never seen an initial period of flaccidity as Fulton<sup>3</sup> has observed, and the recovery of motor power after operation has conformed to the original observations of Horsley<sup>1</sup> and of Leyton and Sherrington,<sup>4</sup> recently reviewed by Walshe.<sup>5</sup> The

proximal joints have always recovered first, movements of the digits later, and finer movements of the fingers never return completely, though all patients have been able to return to their former occupations.

The ultimate test of the value of any method of treatment must, of course, be based on the clinical results obtained. It is quite generally recognized that the evaluation of procedures used in the treatment of any form of epilepsy is very difficult, for one can only say that the epileptic patient is cured when he dies years later from some other cause and remains free of convulsions up to the time of death. In spite of this difficulty, however, attempts at evaluation are necessary to decide whether or not a procedure is worthy of continued use, and such an attempt will be made for the Horsley operation on the basis of the results which we have obtained up to this time.

In the series of sixteen cases of subpial resection (table 1) there have been two deaths. One (patient 1<sup>2</sup>)

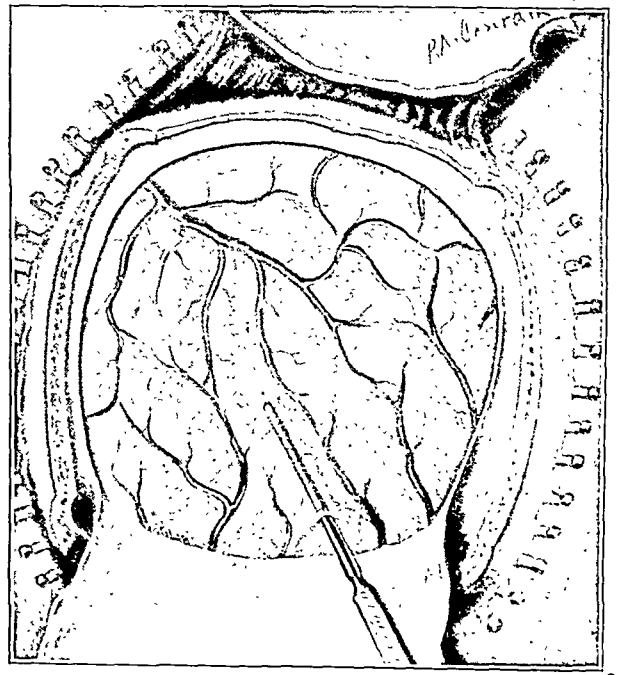


Fig. 1.—Method of freeing the pia.

died of an infection following laminectomy for posterior root section about two weeks after the subpial resection. The other patient developed an extradural postoperative clot and in spite of the removal of the clot died forty-eight hours after the original operation. The mortality rate for the series is 12.5 per cent.

So far as we have been able to determine, seven, or 43 per cent, of the patients have had no recurrence of convulsive seizures for periods ranging from four to twenty-three years. Thus we might claim a 43 per cent "cure." However, we still adhere to the definition of a "cure" for epilepsy as previously given.

In six cases there has been a recurrence of convulsive seizures, but in five instances the convulsions have been less severe, and every patient has been able to resume his former occupation. In three of these cases the attacks before operation were definitely jacksonian as to origin, but with the spread of the convulsion unconsciousness developed. Since operation, with one exception, the attacks which recurred have remained focal and consciousness has been retained.

3. Fulton, J. F.: Forced Grasping and Groping in Relation to the Syndrome of the Premotor Area, *Arch. Neurol. & Psychiat.* 31: 221 (Feb.) 1934.

4. Leyton, A. S. F., and Sherrington, C. S.: Observations on the Excitable Cortex of the Chimpanzee, Orang-Utan and Gorilla, *Quart. J. Exper. Physiol.* 11: 135, 1917.

5. Walshe, F. M. R.: On the "Syndrome of the Premotor Cortex" (Fulton) and the Definition of the Terms "Premotor" and "Motor," with a Consideration of Jackson's Views on the Cortical Representation of Movements, *Brain* 56: 49 (part 1) 1935.

In one case there has been no improvement, in that the attacks occur about as often as before operation and are just as severe. This case is an excellent example of poor selection, as the following brief summary will show:

Ten years before the entry of L. T. O., a man aged 23, admitted Jan. 24, 1938, his mother noticed a twitching of the muscles around the right corner of the mouth. The patient

hours, however, but for about ten days after operation there was some speech disturbance, chiefly in the enunciation of labials and sibilants, especially those occurring at the end of a word.

The patient was discharged on the thirteenth postoperative day and up to that time had had no more attacks. However, since discharge he reports by letter that both major and minor attacks have recurred and are about as frequent and severe as before the operation.

In the first place it was questionable, at least to some members of our staff, whether this case was one of true focal epilepsy. The minor attacks seemed purely subjective for no twitching was visible, and in the major attacks the spread was so rapid that it closely resembled general epilepsy.

In the second place the motor speech area, which of course could not be removed, seemed as much a focal

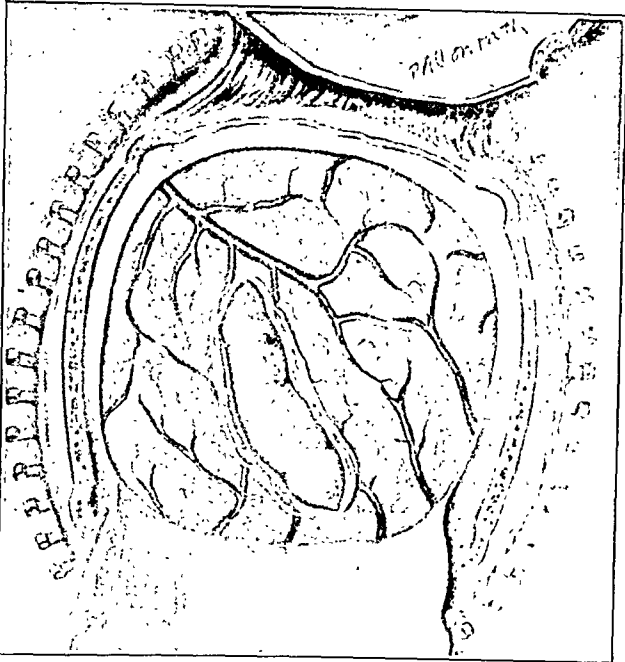


Fig. 2.—The convolution completely freed after the pia arachnoid has been pushed back with cotton pledgets.

was not aware of this twitching, nor was it noticed by other members of the family or by friends. This continued at intervals of two or three months for three years, when, without warning, the patient had an attack which began with drawing of the mouth to the right, but the attack spread very rapidly to become a generalized convulsion with loss of consciousness and ensuing stupor. Similar attacks recurred at frequent intervals, and three years before admission a left cerebral craniotomy was carried out elsewhere with no postoperative improvement.

TABLE 1.—Subpial Resection of Cortex

Diagnosis	Number	Deaths	"Cured"	Improved	Unimproved
Athetosis.....	2	1	1		
Focal epilepsy.....	14	1	7	5	1

The major attacks at the time of admission occurred about once each week and there were numerous minor attacks in which the patient was unable to speak and felt a twitching about the right corner of the mouth. However, this twitching could not be seen by the examiner.

Encephalography gave no evidence of a tumor nor could any other focal lesion be demonstrated. The attacks promptly recurred after encephalography. It was thoroughly explained to the patient that the results were uncertain because of the proximity of the motor speech area to the motor face center, but he was anxious for any procedure offering a chance of relief, so craniotomy was done under local anesthesia. With galvanic stimulation an area was found which produced movements of the right side of the face, jaw and throat. The patient said that this was identical with his minor attacks. A subpial resection of this area was carried out, and immediately following operation there was a slight cortical type of right facial weakness. This disappeared after twenty-four to forty-eight

TABLE 2.—Subpial Resection of Normal Cortex for Focal Epilepsy

Number	Motor	Motor and Sensory	Deaths	No Convulsions	Convulsions Decreased	Unchanged
8	6	2	1	1	5	1

point as the face center, so it was doubtful whether removal of the face center alone would help. The subsequent course has proved that conservatism would have been the wiser policy.

In reviewing these cases it is of interest to determine the result obtained in the eight cases in which there was a perfectly normal cortex with no history of preceding trauma (table 2). Three of these are included in the

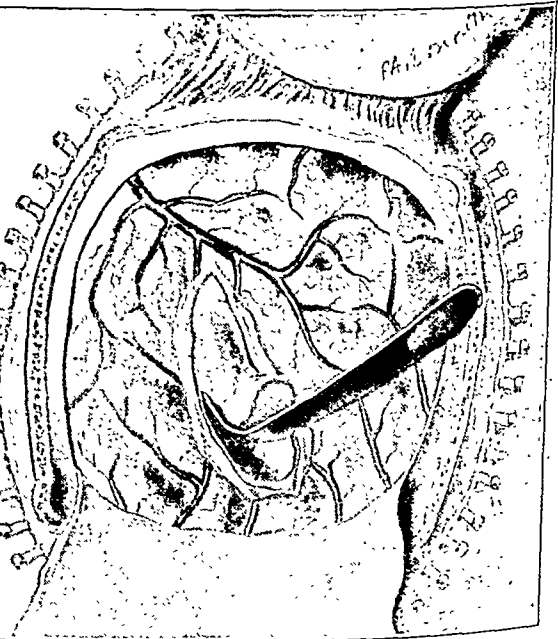


Fig. 3.—Removal of the convolution after the pia arachnoid has been pushed back. This is an absolutely bloodless procedure.

previous report<sup>2</sup> and there have been five additional cases since that time. Of these eight patients one died shortly after operation, so that the mortality rate is the same as for the entire series, 12.5 per cent. In one case, already cited, no improvement occurred. Of the remaining six patients, one has been entirely free from

attacks for fifteen years and the other five have been able to resume their former occupations. In all cases the postoperative attacks have been less frequent and severe, and in only one has there been a progression to a generalized convulsion, and whereas this patient had twelve grand mal seizures in the year before operation he has had only two in the twelve months period since operation.

It is very important that these patients be given careful instructions as to the continuance of sedative drugs after operation. We use phenobarbital in small doses in every instance for many months even though there is no recurrence of attacks. The dosage may usually be greatly reduced as compared to the amount taken preoperatively, but several of our patients have had attacks only after disregarding orders and omitting medication.

One may only speculate as to future developments in this procedure. Even a casual comparison between this and the former report<sup>2</sup> will show that the results now are statistically less impressive than at that time. It is our feeling that this holds true of many methods of treatment, especially those dealing with epilepsy; viz., the longer the period of observation the lower the percentage of cures. The fact that the paralysis produced after cortical excision is only temporary is highly suggestive that motor innervation comes, at least in part, from adjacent convolutions, and we may not have been radical enough. It is our hope that studies of the electrical potentials of the exposed brain, such as we are now carrying out in a routine manner, will give a better understanding of the underlying etiology and pathology of epilepsy, and thereby assist in improving the therapy.

#### SUMMARY

In sixteen cases in which a subpial resection of an area of cortex (Horsley operation) has been done there have been two deaths, giving a mortality rate of 12.5 per cent. Seven patients have been, up to the present time, entirely relieved of attacks. Six patients have shown very definite improvement. In one case there has been no change.

#### ABSTRACT OF DISCUSSION

DR. R. G. SPURLING, Louisville, Ky.: I have done subpial resection on parts of the true motor cortex in which disease was not obvious in three instances. In one there has been complete relief of all convulsive phenomena for four years and in another great improvement, while in the third the result has been indifferent. I should like to ask whether all the excised tissue has been studied with serial sections. It must be remembered that most of the true motor cortex, area 4, in human beings, particularly the lower half, is folded into the sulcus. It seems to me therefore that it would be a difficult surgical feat to limit the excision sharply to area 4 without considerable damage to area 6. Unless Dr. Furlow can demonstrate histologically with serial sections that the resection does not encroach on area 6, I do not feel that he has sufficient evidence to challenge Dr. Fulton's observations on flaccidity and spasticity.

DR. LEONARD T. FURLOW, St. Louis: In the cases reported there was a rather prolonged preoperative period of treatment with drugs, and only after it was determined conclusively that the condition was not controlled by drugs was the patient submitted to operation. In regard to Dr. Spurling's question as to the histologic studies of the specimens removed: Serial sections were examined by Dr. O'Leary of the department of cytology, who, we feel, is much more capable of expressing a definite opinion than are we of the department of neurosurgery, and he assures me that there was an accurate excision of the motor cortex.

## THE MANAGEMENT OF EXTERNAL INTESTINAL FISTULAS

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AND

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Intestinal fistula may be defined as an abnormal communication between a portion of the intestinal tract and a hollow abdominal viscus (internal fistula) or between a segment of the intestine and surface of the body (external fistula).

#### CLASSIFICATION AND ETIOLOGY

From an etiologic standpoint, intestinal fistulas may be placed in two general groups: (1) those which are intentionally established by such operations as colostomy, enterostomy or appendicostomy and (2) those which are produced by some pathologic process or by trauma, for example actinomycosis, tuberculosis, regional enteritis, a malignant condition, gunshot or penetrating wounds or surgical accidents. The fistulas which arise as a result of inflammatory disease are most frequently the sequelae of appendicitis, diverticulitis and pelvic inflammatory processes. Similar classifications have been suggested by Rigby<sup>1</sup> and Coffey.<sup>2</sup>

In a review of 109 cases of fecal fistula collected from the records of Johns Hopkins Hospital from 1891 to 1931, Lewis and Penick<sup>3</sup> made the following classification: (1) subsequent to appendicitis (44.9 per cent), (2) associated with other infections (12.8 per cent), (3) attributable to malignancy (2 cases), (4) resulting from trauma and nonoperative measures (5 cases), (5) following operations (19.2 per cent).

It has been estimated that approximately 4 per cent of cases of appendicitis are followed by fecal fistula. Many such fistulas communicate with the cecum. In recent years it has been observed that a considerable number of fistulas follow removal of an inflamed appendix in cases in which terminal ileitis or typhlitis is present. A fecal fistula may follow evacuation of an appendiceal abscess in cases in which it does not seem feasible to remove the remnant of appendix at the primary operation. A fecalith in the remaining portion of the appendix may be responsible for the formation of such a fistula. There have been strong arguments both for and against inversion of the appendiceal stump. According to experience at the Mayo Clinic, inversion of the stump by means of silk ligatures has been satisfactory, for we have not observed a case in which the edematous cecal walls have become necrotic and have sloughed, as has been reported in some articles. Lewis and Penick<sup>3</sup> mentioned only five instances in which fecal fistula followed inversion of the appendiceal stump in several thousand cases in which appendectomy was performed at the Johns Hopkins Hospital. Of course, especial care should be exercised

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Read before the Section on Surgery, General and Abdominal, at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 17, 1938.

1. Rigby, H. M.: A Clinical Lecture on Intestinal Fistula, Clin. J. 38: 289-297 (Aug. 16) 1911.

2. Coffey, R. C.: Remote or Indirect Subperitoneal Drainage in the Extraperitoneal Closure of Persistent Fecal Fistulae, Ann. Surg. 45: 827-835 (June) 1907.

3. Lewis, Dean, and Penick, R. M., Jr.: Fecal Fistulae, Internat. Clin. 1: 111-130 (March) 1933.



in suturing the inflamed intestinal walls. Catgut sutures are employed if definite typhlitis is present.

The drain employed at an abdominal operation may be responsible for postoperative fistula. However, practically every writer on the subject has concluded that the use of drainage material is definitely indicated under such conditions as that of appendical abscess. Hard rubber drains may produce pressure necrosis of a portion of intestinal wall and give rise to fistula. A fistula is likely to follow any extensive operation in the presence of infection or potential infection. Retained gauze sponges, unabsorbed ligatures, parts of surgical instruments or fecaliths may be the cause of failure of a surgical wound to heal.

Incomplete removal of a diseased portion of intestine may be followed by a postoperative sinus or such a condition may ensue from disturbance of the blood supply or other operative trauma. Injury to the duodenum giving rise to fistula may occur during removal of the right kidney. W. J. Mayo<sup>4</sup> reported three such cases, in all of which there was fatal issue. He called attention to the danger of blindly attempting to control hemorrhage with heavy forceps. Injury to the duodenum may occur during operation on the gall-bladder, in the presence of anomalies or extensive adhesions which require considerable dissection. A fistula sometimes develops after repair of a hernia and following pelvic operation, especially if the latter is concerned with inflamed adnexa.

A number of other causes of intestinal fistula have been recognized: Regional enteritis, affecting either the small or the large intestine, may produce fistula and in many instances a tract develops as a result of localized abscess following perforation of the diseased intestinal segment. Foreign bodies within the lumen of the bowel may be responsible for perforation and the production of fistula. Abdominal injuries, such as gunshot or stab wounds, may lead to formation of fistula as a result of some damage to the adjacent bowel or to its blood supply. Strangulated hernia may have a similar effect. A blow on the abdomen may cause injury to a viscus (for example, the retroperitoneal portion of the duodenum) even though the abdominal wall has not been penetrated. Congenital intestinal fistula is a rare sequence of failure of the vitello-intestinal duct to close.

#### SYMPTOMS AND CONSTITUTIONAL EFFECTS

The primary factor which determines the local and constitutional effect of the fistula is the segment of intestine involved. The nearer the opening in the intestine is to the pylorus, the greater is the power of the intestinal contents for digestion of the skin and the more profound is the constitutional effect from loss of electrolytes. The size of the fistulous opening is not as important as the amount of fluid that is lost, and these features are not necessarily comparable since large quantities of fluid may escape through a small opening in the duodenum while a huge colonic stoma may have comparatively slight local or constitutional effects so far as loss of fluid is concerned. As Kanavel<sup>5</sup> and Dixon<sup>6</sup> have shown, severe toxemia is produced

by loss of a large amount of the biliary and pancreatic secretion. Walters and Bollman<sup>7</sup> and Walters, Kilgore and Bollman<sup>8</sup> have shown that the same effects ensue from obstruction high in the intestinal tract; namely, there is an increase in blood urea and in the carbon dioxide combining power of the plasma and a decrease in the chlorides of the blood. If the fistula arises high in the intestinal tract, as in the duodenum or jejunum, there is usually marked irritation of the skin and excoriation as a result of the action of trypsin, which is secreted as trypsinogen and is activated by the enterokinase of the duodenal secretion. As much as 4 liters of fluid may be lost daily through such a fistula. The loss of gastric secretions alone results in alkalosis, while loss of the pancreatic secretions alone will tend to result in acidosis; in many cases the presence of a fistula diverts quantities of both to the surface.

#### DIAGNOSIS

The diagnosis of intestinal fistula usually is not difficult to make, although Baldwin<sup>9</sup> expressed the belief that the odor of infection caused by the presence of colon bacilli in the wound and that of fecal material discharged through a fistula might easily be confused by those not familiar with either condition. In some instances in which the opening in the intestine is minute and the amount of drainage small, a history of the passage of gas through the tract helps to establish the diagnosis or the taking by mouth of a dye such as carmine red may reveal whether the conclusions as to the presence of fistula are correct. Judd<sup>10</sup> suggested injection of an opaque medium into the sinus and plugging the opening. After this the patient is given a purge and subsequently the course of the substance is observed roentgenologically. If the medium appears in the bowel, the presence of an intestinal fistula is established. Purulent material mixed with the fecal discharge indicates infection or abscess about the sinus.

#### PROGNOSIS

Prognosis depends largely on the site of origin of the fistula; that is, the prospect of cure increases with proximity of the fistula to the anus. Colp<sup>11</sup> reported a mortality rate of 51 per cent in cases of duodenal fistula, with death occurring as early as three days subsequent to formation of the tract. Fistulas of the upper part of the intestinal tract do not heal spontaneously so often as do those which arise from the more distal segments of bowel. Lewis and Penick<sup>12</sup> reported a mortality rate of 8.9 per cent from surgical closure if the sinus tract was long and was lined by granulation tissue. MacLaren<sup>13</sup> found that 19 per cent of seventy-seven patients died following closure of sinuses that appeared after appendectomy but Deaver<sup>14</sup> reported a mortality rate of 49 per cent in 222 such cases in which operation was required. In ten of the 222 cases the sinus recurred but in most instances

4. Mayo, W. J.: *Accidental Injuries to the Descending Portion of the Duodenum During Removal of the Right Kidney*, J. A. M. A. 62: 343-345 (Jan. 31) 1914.

5. Kanavel, A. B.: *Duodenal Toxemia Following Rupture of the Duodenum, with Remarks on Extraperitoneal Rupture and a Report of Two Cases*, J. A. M. A. 62: 759-761 (March 7) 1914.

6. Dixon, C. F.: *The Value of Sodium Chloride in the Treatment of Duodenal Intoxication*, J. A. M. A. 82: 1498-1502 (May 10) 1924.

7. Walters, Waltman, and Bollman, J. L.: *The Toxemias of Duodenal Fistula: Physiologic Changes Concerned in the Production of Its Characteristic Chemical Reactions of the Blood*, J. A. M. A. 80: 1847-1853 (Nov. 26) 1927.

8. Walters, Waltman; Kilgore, A. M., and Bollman, J. L.: *Changes in the Blood Resulting from Duodenal Fistula: A Clinical and Experimental Study*, J. A. M. A. 86: 186-189 (Jan. 16) 1926.

9. Baldwin, J. F.: *The Prevention of Fecal Fistula After Appendectomy: Simple Ligation vs. Precarious Purse-String*, Ann. Surg. 95: 704-714 (May) 1932.

10. Judd, E. S.: *Personal communication to the authors.*

11. Colp, Ralph: *External Duodenal Fistulae*, Ann. Surg. 78: 725-744 (Dec.) 1923.

12. MacLaren, Archibald: *The Closure of Fecal Fistulae*, J. Am. Med. Assoc. 34: 185-189 (April 1) 1918.

13. Deaver, J. B.: *External Fecal Fistula Following Appendectomy*, Ann. Surg. 83: 782-789 (June) 1926.

healing was spontaneous. Rankin and Gorder<sup>14</sup> reported twenty-seven deaths in 264 cases in which 79 operations were performed, a mortality rate of 0.2 per cent.

#### MEDICAL TREATMENT

The aim of medical treatment is to prepare the patient for surgical closure of the fistula and to promote spontaneous closure by making conditions favorable for it. Many of the fistulas from the upper part of the intestinal tract can be caused to heal by this method.

A low residue, high caloric type of diet is employed. The site and character of the fistula must be established and the presence or absence of obstruction in the distal loop must be determined by roentgenologic studies. It is essential to detect and correct the chemical or fluid imbalance that so frequently occurs. The loss of chlorides and of water associated with fistula high in the intestinal tract can be compensated by intravenous administration of physiologic solution of sodium chloride and by use of salt in every possible way. If the proximal and distal loops can be recognized, loss of electrolytes will be prevented by collecting the fluid which drains from the proximal loop and injecting it into the distal segment of the intestine.

Excoriation of the skin which accompanies high intestinal fistula is the factor of greatest concern to the patient and, from the physician's standpoint, it is perhaps the most emergent condition at the beginning of the treatment. That this excoriation is extremely difficult to control is evidenced by the multiplicity of apparatus, devices and medication advocated for its relief. Constant suction seemingly gives the most nearly universal relief, as it removes the offending fluid before it attacks the cutaneous margin. A type of intermittent suction which gives considerable promise of being effective has been described recently by Tenopyr and Shafiroff.<sup>15</sup> If dressings are applied the offending fluid is retained in proximity to the skin and maceration is encouraged. A lighted hood keeps the skin dry, the lights may help to prevent action of enzymes on the skin, and a feature of importance is that a dressing is unnecessary. Frequent tub baths often are of material aid in relieving distress from excoriation.

CoTui<sup>16</sup> experimented with kaolin in the care of high intestinal fistula. The object was to remove trypsin by means of particles of kaolin which have a different electrical charge than that of the enzymes. According to experience at the clinic, a useful method of protecting the skin from the digestive action of enzymes is to place a suction tube through a wall that is built around the external stoma. This wall is made of adhesive tape and a paste composed of kaolin and water (fig. 1). Kaolin powder is used advantageously in this way. Occasionally an ointment made of kaolin and liquid petrolatum or kaolin and zinc oxide is effective in protecting the skin. First the abdominal wall is cleansed thoroughly with ether to remove all grease and to allow adhesive tape to stick to the tissues more firmly. In building the wall to which reference has just been made, the tape is applied about 2 inches (5 cm.) from the central opening; then the skin in

the enclosure is covered with powdered kaolin before any further fluid is discharged from the opening. The small amount of moisture in the skin is sufficient to cause a coating to form immediately and to protect the excoriated skin. Kaolin paste is then added at the periphery, forming a well, the bottom of which is the fistulous sinus. Sometimes, because of the extreme sensitiveness of the excoriated skin and consequent apprehensiveness of the patient, it is advisable to induce sleep for a few moments by giving thiopentothal intravenously. An opening is made in one side of the improvised wall and a fenestrated, soft rubber tube is so inserted that one end is outside and one is more or less inside the external stoma of the fistula. This permits aspiration of the fluid that drains forth without sucking the mucosa into the tip of the tube, thus plugging its lumen and possibly damaging the bowel. The solid cake of kaolin protects the epidermis. If the

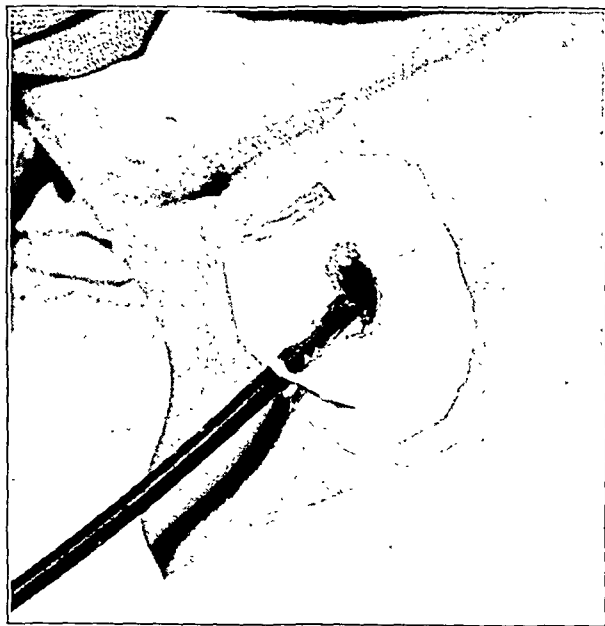


Fig. 1.—Method of protecting skin by means of a suction tube inserted through a wall that encircles stoma.

cake of kaolin becomes undermined, it is removed, the area is cleaned and the process of caring for the fistula is repeated.

Plugging of the suction apparatus with mucosa or intestinal content is a handicap. Bohrer and Milici<sup>17</sup> inserted a fenestrated rubber tube a half inch in diameter into the fistulous tract to act as a reservoir, which is emptied by a smaller tube, thus preventing damage to the mucosa from suction and obviating plugging of the apparatus. This seemed to be a logical procedure and it was tried but the holes in the larger fenestrated tube became plugged. Potter<sup>18</sup> employed a Bradford frame on which the patient lay prone; in this method an opening through the frame permits drainage to take place into a bedpan. Some prolapse of the mucosa prevents the secretion from coming in contact with the skin. The frame is used at night and during periods of rest in the daytime; at other times continuous suction, which the patient manipulates, is available. The rubber tube is provided with a glass

14. Rankin, F. W., and Gorder, A. C.: Fecal Fistula, in Rankin, F. W.; Bergen, J. A., and Buie, L. A.: *The Colon, Rectum and Anus*, Philadelphia, W. B. Saunders Company, 1932, pp. 346-358.

15. Tenopyr, Joseph, and Shafiroff, Benjamin: High Intestinal Fistula: A Method of Treatment, *Ann. Surg.* 105: 477-480 (March) 1937.

16. CoTui, F. W.: The Excoriations Around External Gastrointestinal Fistulae: Experimental Studies on Their Etiology and Further Experience with the Kaolin Powder Treatment, *Ann. Surg.* 98: 242-248 (Aug.) 1933.

17. Bohrer, J. V., and Milici, Attilio: Duodenocutaneous Fistulae, *Ann. Surg.* 93: 1174-1190 (June) 1931.

18. Potter, E. B.: Intestinal Fistulae: A Method for Preventing Digestion of the Skin, *Ann. Surg.* 95: 700-703 (May) 1932.

tip so that plugging can be readily detected and remedied. To prevent plugging of the tube we have used a modified rectal drip apparatus; the escaping intestinal content is diluted by the saline solution thus provided and opportunity for occlusion of the suction tube is decreased.

Just recently we cared for a patient who had a fistula originating in the distal part of the jejunum; this had followed an abdominal operation performed elsewhere. There was marked destruction of the tissues surrounding the enteric stoma; the subcutaneous tissues had been digested and excoriation involved the entire left anterior abdominal wall. Obviously, the patient suffered constantly from excruciating pain and the use of a narcotic was required for relief. Since the denuded area was so large it seemed impracticable to attempt to build the usual kaolin dam or well; instead, a 10 per cent solution of tannic acid was sprayed over the tissues with an ordinary atomizer. Immediate relief followed. A tube was inserted a short distance into the fistula for the purpose of drainage and aspiration. The previous loss of fluids was made up by intravenous administration of saline and dextrose solution. Ten days later, surgical closure of the fistula was effected. Employment of tannic acid in such cases is suggested as a means of obtaining at least temporary relief from the distress which accompanies excoriation.

From the number of devices that have been advocated, it is evident that there is no method that is satisfactory in all cases. Erdman<sup>19</sup> treated a duodenal fistula by means of an apparatus for continuous suction, which he suspended from a semicircular rod designed by Pool. Ochsner<sup>20</sup> administered egg white orally and this was successful in lessening excoriation. Cameron<sup>21</sup> reported closure of a duodenal fistula in eleven days following continuous use of suction through a catheter placed in the opening of the fistula. Judd<sup>10</sup> and we have also treated several duodenal fistulas successfully by this method. Rees<sup>22</sup> obtained a satisfactory result by employment of dressings of commercial dried whole milk. Potter<sup>23</sup> advocated a solution of beef broth and tenth normal hydrochloric acid, with subsequent use of commercial peptone solution (Witte's) to absorb the enzymes. Warshaw and Hoffman<sup>24</sup> introduced hydrochloric acid directly into the sinus and kept the adjacent skin bathed in Witte's peptone solution. The injection of bismuth paste still has its proponents. Cushing<sup>25</sup> advocated a continuous bath and Ochsner<sup>26</sup> stated that a patient of his was saved by this method.

From time to time plugging of the external opening of the sinus tract has been advocated. This is definitely contraindicated in the presence of inflammation. The plugs have been made of various materials, ranging from ordinary gauze packing to tampons of iodoform gauze impregnated with 10 per cent camphorated oil to prevent saturation with secretion and to preclude

also the concomitant maceration. Chewing gum has been employed as a plug. Of course all such plugs are kept firmly in place by a sponge held in situ by adhesive tape or by a tight belt or binder. A few years ago we cared for a patient who had had a large enteric fistula for three years. Numerous attempts to secure closure by surgical intervention had been futile. He was induced to try plugging the stoma with chewing gum. After he had chewed four or five sticks of gum to extract the sugar, the gum was molded into a closed cone, the long end of which was inserted into the fistulous opening while the flange was compressed against the skin of the abdomen. In this manner the escape of enteric content could be prevented for many hours and the patient was afforded a degree of comfort he had not experienced in many years. Subsequently, this method has been employed many times in dealing with small fistulas. It is not proposed as a curative maneuver but it is mentioned as a means of preventing the escape of intestinal content. This accomplishes a double purpose: prevention of dehydration and of irritation of structures adjacent to the stoma. Any plan that will accomplish these objects obviously is of great aid in preparing patients for operation. According to Ochsner,<sup>26</sup> Reyband in 1827 advocated the insertion of wood or ivory plates into the fistulous opening and Kleybolte in 1842 described two leather disks connected by a thread which were used for the purpose. Recently Hartzell<sup>27</sup> has reported the use of a device which appears to be an elaboration of the plan of Reyband.

A large, flexible, rubber T-tube has been devised especially for use in the treatment of fistulas of the spur or hernial type. The original T-tube used by Koehler<sup>28</sup> utilized the entire tube. An advantageous modification has been effected by cutting the vertical limb horizontally, forming a gutter instead of a canal from that portion of the tube which is within the lumen of the bowel.

Fistulas which are distinctly more proximal to the anus (frequently referred to as "low" fistulas) heal spontaneously in from 39 to 88 per cent of cases; hence conservative measures should be tried for from six to twelve months before radical methods are employed. The length of time operation can be deferred judiciously is governed by the amount of inconvenience the patient suffers because of the fistula and by his general condition. Before undertaking conservative measures, the possibility of the existence of obstruction below the fecal stoma must be eliminated. Not infrequently a foreign body, such as a sponge, fecalith or a piece of unabsorbed suture material may be responsible for failure of the sinus to close. Epithelialization of the sinus tract can be prevented by employing silver nitrate. It has been reported that obliteration of the sinus tract has followed insertion and retention of a silver nitrate stick in the fistulous tract for a time. However, an ordinary gauze sponge frequently will accomplish the same result. If the opening of the sinus is large, it is advisable to anchor the plug firmly to the skin by string and strips of adhesive tape; an ordinary sea sponge can be used to cover the taped plug and produce pressure.

Before attempting to close a low fistula, the intestinal content should be evacuated thoroughly by means of

19. Erdman, Seward: Laceration of Duodenum; Rupture of Liver; Duodenal Fistula: Jejunostomy Feeding; Parotiditis; Recovery, *Ann. Surg.* 73: 793-797 (June) 1921.

20. Ochsner, A. J.: Intestinal Fistula, *S. Clin. Chicago* 3: 699-703, 1919.

21. Cameron, A. L.: The Treatment of Duodenal Fistula, with Report of a Case, *Surg. Gynec. & Obst.* 37: 599-606 (Nov.) 1923.

22. Rees, C. E.: Dried Milk as a Dressing for Intestinal Fistula: Report of Case, *California & West. Med.* 30: 419 (June) 1929.

23. Potter, C. A.: Treatment of Duodenal and Fecal Fistula: Further Observations, *J. A. M. A.* 92: 359-363 (Feb. 2) 1929.

24. Warshaw, David, and Hoffman, W. J.: High Intestinal Fistula: Report of Case Treated by Modification of Potter Method, *J. A. M. A.* 94: 1050-1052 (April 5) 1930.

25. Cushing: Remarks upon a Case of Jejunal Fistula, *Bull. Johns Hopkins Hosp.* 10: 136-137 (July) 1899.

26. Ochsner, Alton: Intestinal Fistulae, in *Nelson's Loose Leaf Surgery* 5: 295L-296E, 1928.

27. Hartzell, F. B.: The Treatment of Fistulas of the Small Intestine, *Surg. Gynec. & Obst.* 66: 108-116 (Jan.) 1938.

28. Koehler, quoted by Eliot, Ellsworth, Jr.: Fistulae of the Small and Large Intestine, *Ann. Surg.* 86: 406-412 (Sept.) 1927.

irrigation. Frequently it is possible to find the site of involvement by means of roentgenographic studies of the small intestine and colon. For three or four days prior to surgical intervention the patient should be given a nonresidue diet, and a saline laxative is to be employed to promote complete emptying of the intestine. The patient is encouraged to supplement the intake of fluid with sweetened fruit juices and to eat candy; both help to build up a carbohydrate reserve and thus to protect the liver and change the bacterial flora of the bowel. The patient who has an enteric fistula usually is fairly well vaccinated by the infectious process; consequently the antiperitonitis vaccine used as a routine in colonic cases might be eliminated in the preparatory treatment but as an extra precautionary measure it usually is employed.

#### SURGICAL TREATMENT

Jejunostomy of the Witzel type is perhaps the most conservative procedure in the surgical treatment of duodenal fistula. This places the affected segment of intestine partially at rest and permits administration of liquids and nourishment, and introduction of the duodenal secretion obtained by suction. In the absence of some such measure, the duodenal secretion tends to be lost by drainage to the outside.

W. J. Mayo<sup>29</sup> advised a transperitoneal approach for the repair of duodenal fistula resulting from injury received in the course of right nephrectomy. Deaver<sup>30</sup> stated that he had successfully repaired duodenal fistulas soon after their occurrence and that, in his opinion, delay was dangerous. In some cases he amputated the upper part of the duodenum and the pylorus and established a posterior gastro-enteric stoma. According to the experience of surgeons at the Mayo Clinic, application of constant suction frequently will bring about healing of a duodenal fistula. In a few cases in which the sinus persists, the delay affords a better opportunity for surgical intervention to be successful. The fluid balance should be watched carefully. Chemical imbalance in relation to the chlorides of the blood is compensated by giving sodium chloride intravenously or subcutaneously or by jejunostomy tube.

The surgical treatment of low intestinal fistula varies with the size and situation of the stoma. The presence of a spur or mucosa-lined tract almost invariably necessitates surgical intervention, which ranges from the application of spur-crushing clamps to simple closure or extensive resection of the intestine. The best procedure for treatment of a fistula which cannot be cured by medical means is one by which the sinus, and not infrequently the segment of bowel in which it arises, is removed. Lockhart-Mummery<sup>31</sup> said "Operations for closing fecal fistulas are not operations to be lightly undertaken unless one has had special experience. A serious difficulty in connection with these fistulas is that the exact anatomy of the bowel in relation to the abdominal wall cannot from the very nature of things be known with any exactitude." He also called attention to the necessity for intraperitoneal exposure to insure maintenance of the blood supply.

Simple closure of the fistula consists of inversion of the mucosal edges with two or three layers of chronic

catgut and suture of the skin. This procedure is not sufficiently radical to effect cure in every case and it is not advocated unqualifiedly by those who have had extensive experience in intestinal surgery. A more satisfactory procedure is closure by inversion of the mucous membrane and anatomic closure of fascial, muscular and subcutaneous layers.

When radical excision of the sinus and a portion of the bowel is indicated, it is our custom to make an incision which encircles the fistulous opening and extends well beyond the stoma, as this allows sufficient exposure. The sinus should be plugged to prevent spilling and the bowel is dissected free from the abdominal wall. The defect in the bowel is then repaired, either by resecting one or several loops of intestine or by merely closing the opening.

The sinus tract is isolated from the peritoneal cavity and from the incision by warm intestinal packs. A plan we have followed for several years is to apply a Payr clamp across the fistulous tract near the site at which closure is to be made or, if the fistula is small, a Kelly or Ochsner hemostat is used (fig. 2). Then the skin

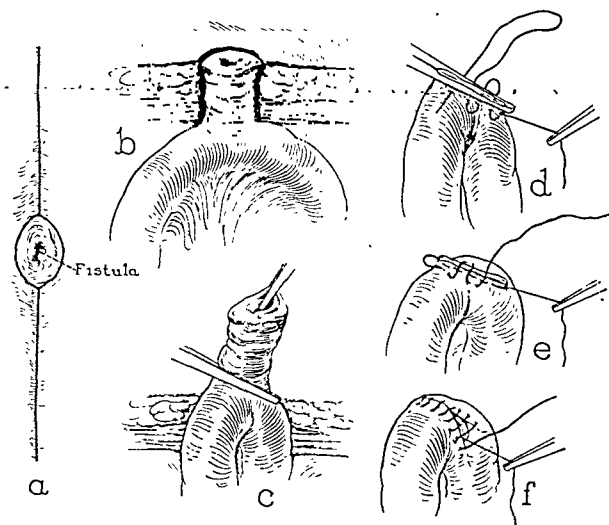


Fig. 2.—Steps in closure of fistula.

and fat distal to or above the clamp are removed by excision with knife or cautery in close proximity to the clamp. After the fistula has been clamped, closure is begun. A through and through running suture is then placed immediately beneath the clamp. Next the clamp is removed. The second row of sutures is placed, a Cushing type of stitch being used to approximate the serosa over the first row of sutures. A third row of sutures may be employed for reinforcement. Then, if possible, a small patch of omentum is placed over the site of closure.

Attention has been called frequently to the importance of maintaining an adequate blood supply in these cases. The bowel should be cut at an acute angle with the mesenteric border, so that more is taken from the antimesenteric border than from the mesenteric side even if it is necessary to sacrifice normal intestine, for an ample blood supply is imperative for satisfactory and permanent closure.

If considerable manipulation of the viscera has been necessary an enteric stoma of the Witzel type, established proximal to the anastomosis, is often apparently a life-saving measure. Deaver<sup>30</sup> used one or more enteric stomas, according to indications.

29. Mayo, W. J.: Procedures Following Nephrectomy: I. The Transperitoneal Closure of Duodenal Fistulas Following Nephrectomy, *J. A. M. A.* 64:953-957 (March 20) 1915.

30. Deaver, J. B.: Gangrene of Appendix Resulting in Colic and Duodenal Fistulae, *Ann. Surg.* 79:605-606 (April) 1924.

31. Lockhart-Mummery, J. P.: Diseases of the Rectum and Colon. Baltimore, William Wood & Co., 1934.

Should several coils of the intestine be involved, resection of the affected segments may entail assumption of an unreasonable risk and the surgeon will display better judgment if he performs a short-circuiting operation by making a side to side anastomosis.

Unless there is considerable infection and formation of abscess about the sinus, closure without drainage of the peritoneal cavity is the rule. Lockhart-Mummery<sup>21</sup> placed a soft rubber drain down to the anastomosis and left the drain in situ for thirty-six hours. In the closure by layers, a portion of a rubber tube can be used outside the external fascia to act as a guide in case of drainage. The multiple retention sutures of the abdominal wall can be removed on or about the fourteenth postoperative day.

Extraperitoneal closure usually is employed for a temporary colonic stoma incidental to resection of a segment of intestine distal to the site of colostomy. An elliptic incision is made around the stoma at a sufficient distance from the opening to include the phlegmonous, gristly border of the skin. This incision is then continued through the fascial layers down to the peritoneum, but opening of the peritoneum is carefully avoided. The surrounding peritoneum is freed, so that there is ample room for the anastomosed bowel in the subfascial space. Since the intestine has not been divided completely, the mesenteric border is intact and the blood supply to the area of anastomosis is usually ample. The edges of the fistula are then trimmed, bleeding is controlled, and the bowel, which has been opened longitudinally, is sewed transversely with chromic intestinal catgut. Next, the layers of fascia are apposed and a split tube is inserted down to the fascia, thus insuring external discharge of drainage in the event leakage should occur through a long sinus tract.

Fecal fistula through the peritoneum following the Lockhart-Mummery type of operation performed because of a malignant condition of the lower part of the colon or rectum usually can be prevented by keeping the distal loop of intestine empty by means of irrigation. Should a sinus occur, daily irrigation frequently is sufficient to bring about spontaneous closure. A soft cotton plug, inserted into the stoma of the distal loop and anchored to the skin with a piece of string and adhesive tape, is an advantageous adjunct. A more radical measure, but one which is seldom necessary, is inversion and resection of the distal loop of the intestine.

#### POSTOPERATIVE CARE

Constant attention to many details is essential in the postoperative care of patients who have fistula of whatever origin. Immediately after operation the patient is allowed one-half ounce (15 cc.) of any "nonresidue" liquid every half hour, as tolerated. On the second postoperative day, 2 ounces (60 cc.) of liquid is given each hour; on the third postoperative day the amount of fluids is increased to 3 ounces (90 cc.) each hour; on the fourth postoperative day a full nonresidue liquid diet is permitted and the quantity is increased every third day until the tenth postoperative day, when a slightly modified general diet is provided. Daily, 2,000 cc. of 5 per cent dextrose in physiologic solution of sodium chloride is given intravenously or physiologic solution of sodium chloride is administered by infiltration.

Oral hygiene is important, especially if the patient is debilitated; he is encouraged to chew slices of orange or lemon and gum to prevent parotitis. When the

pulse rate is 72 or less per minute, 2 grains (0.12 Gm.) of thyroid extract is given three times daily as long as the beats are less than 100 a minute or until the patient is out of bed.

Liquid petrolatum is given twice daily, beginning on the fourth postoperative day. Three or 4 ounces (90 or 120 cc.) of olive oil is inserted into the rectum daily to prevent fecal inspissation or impaction. Irritant enemas are not given at any time. Vigilance with regard to this restriction is worthy of emphasis.

Restricted exercise is thought to be of distinct advantage and the patient is encouraged to turn in bed frequently and to move the arms and legs freely. He is also advised to take deep breathing exercises. The patient is permitted to sit up with his feet dangling over the side of the bed on the seventh postoperative day; the next day he begins to sit in a chair. Usually it is possible to dismiss the patient from the hospital sometime between the tenth and fifteenth postoperative days.

#### SUMMARY AND CONCLUSIONS

1. The most common cause of intestinal fistula is appendical infection. Many such fistulas are the result of nonspecific granulomas of the cecum and terminal part of the ileum.

2. Many fecal fistulas will close spontaneously within a few weeks. If the general condition of the patient warrants, many weeks should elapse before surgical intervention is undertaken.

3. Injury to the duodenum, with formation of fistula, is a serious and frequently fatal complication of renal and biliary surgical operation.

4. The mortality from repair of fecal fistulas ranges from 8.9 to around 50 per cent. Colp reported a mortality rate of 50 per cent from duodenal fistula occurring as a postoperative complication.

5. The prevention of epithelial excoriation with the use of some type of suction apparatus is a distinct advance in treatment.

6. If simple measures have been given a trial and are unsuccessful, some type of radical procedure should be instituted.

7. Careful preparation and postoperative care are essential.

#### ABSTRACT OF DISCUSSION

DR. GUNTHER W. NAGEL, San Francisco: The authors have presented their subject with their usual thoroughness and candor. Their observations are of special value because they are based on a large experience. The subject is not controversial, so that discussion is largely limited to emphasizing certain points. The subject may be divided into two main groups: prevention and treatment. Of these, prevention deserves special emphasis. In order to prevent intestinal fistulas, their cause must be determined. There are many causes, not all of which can be discussed at this time. In the experience of the authors, previous surgical procedures play an important part. In this group there must be considered again those which might have been prevented and those which arise in spite of one's best efforts. Certain lesions which are prone to result in fistulas if not recognized and properly handled are the group which are now classified as regional enteritis. This is a subject which has been widely discussed in recent years. In the treatment it is important to ascertain the approximate location of the fistula, the length of the tract, the underlying pathologic lesion and its extent, particularly if there is obstruction distal to the lesion. Preoperative methods occasionally result in spontaneous closure of the fistula. Important here are protection of the skin in high intestinal fistulas and replenishment of body fluids and chlorides. Suction is of course

important, and various cutaneous preparations are helpful. Such a simple measure as allowing air and light to reach the wound is occasionally neglected. In the operative procedure, two points must be emphasized: The loop of the bowel must be completely freed and any obstruction distal to the fistula must be relieved. If this is not done, failure will result. Intestinal fistulas may be catalogued and classified, but their treatment requires a high degree of surgical judgment and skill.

DR. ALTON OCHSNER, New Orleans: There are two points to which I should like to call attention as regards the conservative treatment of intestinal fistulas. The authors have emphasized the importance of determining the etiologic factor which is of the utmost importance. Most fistulas, however, unless there is a disease process, will heal spontaneously. A relatively simple measure is one I have been using the past year, which was accidentally observed following the diagnostic determination of the extent of a fistula. The introduction of the iodized oil into the fistulous tract in a surprisingly large number of cases will result in a healing of the fistula probably because of its bactericidal activity. It will be recalled that Beck's paste was used for a number of years and quite satisfactorily until the danger of bismuth poisoning was apparent. Iodized oil is perfectly innocuous. It not only determines the extent of the fistulous tract but also aids in the healing process. The authors have referred to the use of bronzing powder. In the clinic in which I work, bronzing powder is used extensively. Relatively recently a patient of mine quite ingeniously hit on a device of applying it which I think is unique. She takes ordinary aluminum paint—her father is in the paint business—and mixes it with cold cream until it has a buttery consistency, so that it can be applied easily to the surface of the skin. This makes an impervious covering which cannot be washed off.

DR. CLAUDE FRANK DIXON, Rochester, Minn.: Dr. Nagel emphasized the importance of attempting to determine the location of the fistula. This, I believe, is an important point and, as a rule, one can determine the segment of intestine from which the fistula arises. Dehydration is one of the greatest problems with which one has to deal in cases of high intestinal fistula. The work of Coller and his co-workers has indeed been of great value in the management of dehydrated patients. They have emphasized, as many know, the importance of supplying a sufficient amount of water so that the urinary output will be around 1,500 cc. a day. This is a good working rule. Their work also has been important in that they show so strikingly that 5 per cent dextrose solution without the addition of saline solution is the solution of choice in supplying liquid to these patients. Unless the blood chlorides are low there is, of course, no reason for the administration of sodium chloride. The care of the excoriated skin surrounding intestinal fistula is many times a great problem. I have used the aluminum paint mixture of which Dr. Ochsner has spoken. My experience has been that it has produced a marked burning sensation to such an extent in some cases that it had to be discontinued. The problem as I see it in dealing with enteric fistulas which require surgical intervention to effect closure is careful preparation of the patient, which means combating dehydration; second, the treatment of the excoriated skin, which in my service has been best managed by the kaolin dam, mentioned previously; and, finally, the use of intraperitoneal vaccine from thirty-six to forty-eight hours before operation.

**Psychopathic Wards in General Hospitals.**—The first psychopathic ward in a general hospital in America fulfilling the function of actual therapeutic treatment besides detention and observation was established at the Albany Hospital in 1902. "Pavilion F" was added to the hospital in that year "for the detention and care of persons afflicted with nervous and mental disorders," on the initiative of Dr. J. Montgomery Mosher, who directed its operation for many years thereafter. Since 1902, psychopathic wards or hospitals have been established in connection with general hospitals in many of the large municipalities. —Deutsch, Albert: *The Mentally Ill in America*, New York, Doubleday, Doran & Co., Inc., 1937.

## RED CROSS BLOOD TRANSFUSION PROJECTS

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Following the example of the British and other European Red Cross societies, the American Red Cross has inaugurated a few blood transfusion services in this country.<sup>1</sup> The first one was started in Augusta, Ga., in May 1937 at the request and with the cooperation of the local physicians and staff of the Georgia State University Medical School and Hospital.<sup>2</sup> Other services have since been inaugurated, among them Baltimore, Paterson (N. J.), Memphis, Chattanooga and Jackson (Tenn.), Little Rock (Ark.), Lowell (Mass.) and Charleston and Aiken (S. C.). Washington, D. C., is about ready to start a campaign for enrolment. A dozen other cities are studying the plan, looking to its final adoption.

The project consists of enrolling volunteer donors who are willing to give blood without a fee for indigent or semi-indigent patients. It is not concerned with professional or paid donors and does not therefore interfere with established paid donor registries now operating in many of the larger cities and hospitals. After the project has been approved by the local physicians, hospitals and other groups concerned, the local Red Cross chapter conducts a campaign for enlisting the donors. They are examined, their blood is typed and if approved they are enrolled. Their names, addresses and telephone numbers are recorded and filed. Then, on receipt of a call from a hospital, the chapter calls a donor of the group requested and makes arrangements to have him transported to and from the hospital. The technical phases of transfusion are a matter for hospital regulation.

The primary objectives in organizing these projects are (a) to meet a widespread need for such services as evidenced by numerous inquiries and requests and (b) to develop a practical plan for operating them on an efficient and more or less uniform basis that does not obtain in volunteer donor services at the present time. Generally speaking, they are quite haphazardly organized and operated. Many communities and hospitals, particularly in the larger cities, have satisfactory registries for paid donors by enrolling so-called professionals, members of the hospital staff, medical students, firemen, policemen and other groups. Comparatively few cities, however, have adequate lists of donors for indigent patients. In most instances doctors appeal to relatives and friends of the patient or draft some one of the hospital staff whose blood has already been typed. As a last resort they sometimes have to make a public appeal through the press or over the radio.

These procedures may result in a rush of volunteers to the hospital, often necessitating grouping a large number before the right type is found; also in a hurried physical examination of the donor to determine his fitness as such. All this is tedious and time consuming and introduces elements of carelessness as well as undesirable heroics. It tends to place mistaken emphasis on the fundamentals of blood transfusion and the value of this important therapeutic measure.

1. Mimeographed Statements, Blood Transfusion Project, American National Red Cross.

2. Brooke, Mildred S.: Augusta Chapter Sponsors Blood Transfusion, Red Cross Courier, September 1937.



Relatives and friends should of course be used whenever possible, provided there is sufficient time for grouping and a careful examination. That is not always possible in emergencies and therefore places a heavy burden on the laboratory and hospital staff. If donors are grouped and examined in advance and the project skilfully managed, the service should become a valuable aid to physicians and hospitals. When blood donors are not readily available the patient often goes without transfusion. That has been brought to our attention by physicians on a number of occasions. Convenience of access and ease of administration multiply the use and effectiveness of any therapeutic measure many fold. Nowhere is this more evident than in blood transfusion.

This is well illustrated by the rapid growth of the British Red Cross service in London, which is perhaps the oldest established community-wide volunteer donor service in the world. It was started in 1921 from very small beginnings as a result of a call for a volunteer donor by one of the hospitals. Its founder, P. L. Oliver,<sup>3</sup> and his associates, recognizing the need for this service and its humanitarian aspects, initiated the plan. It has gradually grown over the years to a well organized and efficient service. In 1925 428 calls were received, in 1930 1,627. Last year 5,622 calls were answered, with an enrolment of 2,475 donors. It is used increasingly from year to year for more patients and for more forms of illness, largely because donors are readily available.<sup>4</sup>

A well planned and directed project of this kind will provide a valuable and convenient service. Physicians are using it now not only in emergencies as they occur in surgery and obstetrics but also in chronic anemias, blood dyscrasias and severe bacterial and chemical toxemias. While the value of transfusion in some of these conditions is still in question, the fact remains that physicians use it in critical illness if donors are available. Since there is a preponderance of illness among indigent and semi-indigent persons, there is greater need for transfusion among this class of patients.

The Red Cross is attempting to meet the need for volunteer donors in communities with a fairly large indigent population where there is no organized registry of this kind. The plan is inaugurated only after a careful study of local needs and facilities and the possibility of competent leadership. The point of view of the local physicians, hospitals and laboratory directors receives first consideration. It is left largely to them to determine whether the project shall or shall not be introduced. Their approval and whole-hearted cooperation is essential. Thus far nearly every study made of the plan in the cities that have adopted it was initiated by physicians or hospital officials and not by the Red Cross. We try to make clear that we are not promoting or urging adoption of the plan but rather that we are willing to organize the project through the chapters if and when the local medical profession and other groups concerned approve and actually want it. We have no other motive than to make this important therapeutic aid available to the doctors and hospitals in communities that need it. It should be stated here that the project is applicable only in communities with adequate hospital and laboratory facilities as well as competent medical direction.

The development of a successful volunteer blood donor project requires careful consideration of many factors relating to management. Paramount among these is the protection of the donor. The patient's interests are of course also important, but these are too self evident to need discussion here; but not so with the donors. When donors are invited to enroll for the specific purpose of giving blood without a fee they must be assured not only of the harmlessness of this procedure but also of a minimum of inconvenience and physical discomfort. It must be remembered that they enlist primarily for humanitarian reasons. They are glad to give blood when needed, provided they have reason to believe it will be put to good use and that their contributions are appreciated alike by doctors, hospital officials and others with whom they come in contact. Unless they are treated courteously from the time they are called to report at the hospital until they return, and unless the technic of taking blood is simple and skilfully performed, they will not continue their names on the rolls. We have learned through experience that to maintain a satisfactory list of donors it is necessary to give them every consideration to which they are entitled.

It is therefore important that certain regulations be instituted within the hospital, governing the handling of donors and standardization of the technical phases of transfusion. These regulations must provide for uniform procedures and technics. The donor should be courteously received when reporting to the hospital. Transfusions should be performed by the indirect or citrate method. Incision of the vein must not be permitted. The caliber of the needle used should not exceed 14 or 12 gage. The donor should be in a recumbent position during venipuncture and in a suitable room not occupied by patients. One or more resident physicians or surgeons thoroughly familiar with transfusion procedures should be assigned to this service. The donor should receive prompt attention and the arm should be properly dressed. He should be dismissed in good condition with an expression of appreciation by the attending physician or nurse. He should be fully satisfied if possible with the treatment accorded him. These are some of the fundamentals necessary for maintaining a successful volunteer donor project. They do not have the same significance when dealing with paid donors.

Then too the chapter must keep in constant touch with the donors by personal visits, letters or telephone calls, must iron out all misunderstandings and complaints and must keep them in a reasonably well satisfied frame of mind. Much detail work is necessary to maintain constantly a satisfactory list of donors and an efficiently functioning service.

Regulations governing the physical examination of donors, grouping and blood tests, equipment, methods and technics to be adopted are all important. These are a responsibility of the physicians and hospitals and must be carefully planned and supervised. It is also necessary to establish some regulation governing the selection of indigent and semi-indigent patients so that the use of volunteer donors will not be abused.

It is the responsibility of the chapter to organize the project, to maintain an adequate list of donors, to transport them to the hospital, to safeguard their interests and to maintain a properly functioning organization day and night. It is the responsibility of the hospitals and

3. Oliver, P. L.: The British Red Cross Blood Transfusion Service, *Guy's Hosp. Gaz.*, March 16, 1935.  
4. Report of the British Red Cross Society for the Year 1937, Blood Transfusion Service, p. 26.

physicians to work out the technical phases of transfusion and to assist the chapters in maintaining high standards of efficiency. Thus far we have experienced little difficulty in enlisting donors and keeping them on the rolls.

Donors are recruited largely from among salaried workers and wage earners. They are usually the stable and respected citizens of the community and constitute a very desirable group both from a health point of view and from willingness to serve. They should preferably be between the ages of 18 and 40, in robust health, free from syphilis and other communicable diseases, and have a readily accessible vein in the arm. A hemoglobin content of 85 per cent and a normal differential blood count with no evidence of blood dyscrasias are required; also a negative Wassermann or other test for syphilis. They should be reexamined every six months or oftener if practicable. A Kahn or similar test and final cross matching with the patient's blood are required at the time of transfusion.

The Baltimore chapter has recently inaugurated a most carefully planned project. It differs from donor services in other chapters in that the entire program is conducted under the direction of a physician employed by the chapter. The donors are all examined and the blood grouped by him and an associate who is especially qualified in hematology. Such a plan should insure an efficient service, although it is applicable only in larger cities. In smaller chapters the project is conducted by the chapter executive and staff of assistants under the direct supervision of a special committee. The chairman of this committee is invariably one of the leading physicians of the community. Here the physical examinations and the laboratory tests are performed on a volunteer basis.

The question is frequently asked as to what relation this donor project has to the development of the so-called blood bank, as originated at the Cook County Hospital, Chicago.<sup>5</sup> The latter is a procedure developed for collecting and storing blood under proper refrigeration until needed for transfusion. Up to the present time Red Cross donors have not been used for filling blood banks. They have been provided only for immediate transfusion purposes. It is possible, however, that in time the project may be modified, particularly for the larger hospitals.

The "blood bank" plan appears to be applicable for the present at least only in larger hospitals where transfusions are a daily occurrence. Since blood cannot be kept for an indefinite period, it might have to be discarded too frequently in hospitals where transfusions are given only occasionally. Wasting blood, particularly when given by volunteers, cannot be permitted. Then too we are not certain that donors would be willing to volunteer so readily if their blood is not to be used immediately. The blood bank may rob the project of some of its humanitarian aspects and thus interfere with the enrolment. Time and experience will determine whether our present project can be modified that way.

The success of the project depends largely on maintaining a constant list of satisfied and willing donors. Anything that may tend to interfere with that should

be carefully studied before it is used. Constant contact with the donors, adding new names to the list from time to time, cautious procedures within the hospital and courteous treatment are all essential. Physicians who use the service must recognize this and do everything possible to help protect the interest of the donor as well as the patient.<sup>6</sup>

## Clinical Notes, Suggestions and New Instruments

### PERIPHERAL NEURITIS DUE TO SULFANILAMIDE

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Current literature records the following reactions to sulfanilamide: agranulocytosis,<sup>1</sup> acute hemolytic anemia,<sup>2</sup> cyanosis,<sup>3</sup> purpuric and scarlatiniform eruptions,<sup>4</sup> exfoliative dermatitis,<sup>5</sup> toxic dermatosis,<sup>6</sup> photosensitization of the skin,<sup>7</sup> fever,<sup>8</sup> sulfhemoglobinemia,<sup>9</sup> methemoglobinemia,<sup>9</sup> optic neuritis,<sup>10</sup> precipitation of a psychosis<sup>11</sup> and the inhibitory action on spermatogenesis.<sup>12</sup> The following report is offered as a probable case of intoxication from the therapeutic use of sulfanilamide:

#### REPORT OF CASE

J. D., a Negro steel construction worker aged 42, was admitted to the neurologic service of Dr. A. M. Ornsteen at the Philadelphia General Hospital Feb. 11, 1938, because of weakness in the hips and legs since January 1. The past medical history was essentially irrelevant. A recently remarried widower, he had one healthy son by his first wife. He stated that he did not use alcohol in any form. With the exception of gonorrhea in June 1936, for which he was adequately treated, he had been well until reinfectd from extramarital exposure in September 1937. At a local hospital he was given 100.5 grain (0.3 Gm.) tablets of sulfanilamide and was told to take three every three hours. His prescription was renewed three times, so that from October 11 to November 15 he took 400 tablets (130 Gm.).

Although the urethral discharge soon ceased, pain and swelling developed in the joints of the legs and arms, and the right eye became inflamed. He was admitted to the genito-urinary ward of the Philadelphia General Hospital November 27. Smear and culture of material from the eye yielded no gonococci. Diagnostic impressions were resolving gonorrheal urethritis, gonorrheal arthritis, nonspecific conjunctivitis and balanoposthitis. He was given approximately four hours of fever therapy

6. References of interest that have not been cited directly:

League of Red Cross Societies Monthly Bulletin, June 1938, p. 86.

Corwin, E. H. L.: Community Control of Professional Blood Donors, New York State J. Med. 35: 317 (April 1) 1935.

Mason, J. M.: Problems of Blood Transfusion, J. Med. 12: 60 (April) 1931.

Stetten, D. Witt: The Blood Transfusion Betterment Association of New York City, J. A. M. A. 110: 1248 (April 16) 1938.

1. Young, C. J.: Agranulocytosis and Para-Aminobenzene Sulfanilamide, Brit. M. J. 2: 105 (July 17) 1937.

2. Kohn, S. E.: Acute Hemolytic Anemia During Treatment with Sulfanilamide, J. A. M. A. 109: 1005 (Sept. 25) 1937.

3. Marshall, E. K., Jr., and Walz, E. M.: Cyanosis from Sulfanilamide, Bull. Johns Hopkins Hosp. 61: 140 (Aug.) 1937.

4. Schonberg, I. L.: Purpuric and Scarlatiniform Eruption Following Sulfanilamide, J. A. M. A. 109: 1035 (Sept. 25) 1937.

5. Myers, G. B., Vonder Heide, E. C., and Balcerski, Matthew: Exfoliative Dermatitis Following Sulfanilamide, J. A. M. A. 109: 1983 (Dec. 11) 1937.

6. Goodman, M. H., and Levy, C. S.: The Development of a Cutaneous Eruption During Administration of Sulfanilamide, J. A. M. A. 109: 1009 (Sept. 25) 1937.

7. Newman, B. J., and Sharlit, Herman: Sulfanilamide: A Photosensitizing Agent of the Skin, J. A. M. A. 109: 1036 (Sept. 25) 1937.

8. Hageman, P. O., and Blake, F. G.: A Specific Febrile Reaction to Sulfanilamide (Drug Fever), J. A. M. A. 109: 642 (Aug. 28) 1937.

9. Paton, J. P. J., and Eaton, J. C.: Sulphemoglobinemia and Methemoglobinemia Following Administration of Sulfanilamide, Lancet 1: 1159 (May 22) 1937.

10. Bucy, J. C.: Toxic Optic Neuritis Resulting from Sulfanilamide, J. A. M. A. 109: 1007 (Sept. 25) 1937.

11. Hogan, B. W., and McNamara, P. J.: Psychosis Precipitated by Sulfanilamide, U. S. Nav. M. Bull. 36: 60 (Jan.) 1938.

12. Jaubert, A., and Metz, C.: Inhibitory Action of Sulfanilamide, and Analogous Drugs on Spermatogenesis, report at the Société médicale des hôpitaux, Dec. 17, 1937.

5. Fantus, Bernard: The Therapy of the Cook County Hospital: Blood Preservation, J. A. M. A. 109: 128 (July 10) 1937. Fantus, Bernard, in collaboration with Schirmer, Elizabeth H.: Blood Preservation Technic, *ibid.* 111: 317 (July 23) 1938. Fantus, Bernard: Cook County's Blood Bank, Mod. Hosp. 50: 57 (Jan.) 1938.

of between 106 and 107 F. in the Kettering hypertherm, after which he felt so much improved that he signed his release from the hospital December 2. He felt well and gained weight until Jan. 1, 1938, when he noticed that his hips and legs were growing increasingly weaker on walking but a short distance, necessitating his sitting down and resting every few steps. His gait finally became so cumbersome that he had to use a cane for assistance. He stated that he felt no pain in the limbs but did note patchy numbness and paresthesias in the distal portions of the lower extremities, more marked on the left. This continued to the date of admission, although it was much improved. The systemic review was essentially negative, with the exception of the yellowness of the eyes during ingestion of the tablets.

The patient was well built and muscular. He was 6 feet 1 inch (185 cm.) in height, without lymphadenopathy; the skeleton was normal. There was no evidence of cyanosis or icterus. Fading maculopapular, erythematous, nonindurated lesions about 0.5 cm. in diameter were situated on the back, in the suprasternal region and above the pubes. The eyes, ears, nose, teeth, tongue and throat were normal with the exception of hypertrophied cryptic tonsils from which no pus could be expressed. There was no tenderness of the nasal sinuses. Examination of the heart and lungs showed that they were entirely normal. The abdominal organs were not palpable. The prostate was enlarged, soft and boggy. The upper extremities were normal. There was no difference in length, size or shape of the lower extremities; abduction of the thighs was markedly weakened. Other muscular movements were good. Moderate compression of the calves and hamstrings elicited sharp pains, more marked on the left. Flexion and extension of the legs on the thighs were well performed, but there was weakness on dorsiflexion of the left foot against slight resistance. Mental examination was negative. Neurologic examination showed a negative Romberg sign and normal cerebellar function. His waddling gait suggested progressive muscular dystrophy; muscular weakness about the pelvic girdle, however, seemed entirely responsible for the disturbed gait, as there was no difficulty in flexion or extension of the back. The cranial nerves were normal. There were no fibrillations. The abdominals, left cremasteric and achilles tendon reflexes were absent. Knee jerks were elicited only slightly on reinforcement. The Babinski sign was not present. All sensory modalities were normal, with the exception of diminution of pinpoint sensitivity below the middle third of the legs.

Examination of the blood revealed red blood cells 4,300,000, hemoglobin content 85 per cent, white blood cells 6,600, polymorphonuclear leukocytes 54 per cent, lymphocytes 42 per cent, monocytes 2 per cent. The Kahn and Wassermann reactions were negative. Examination of the spinal fluid was essentially negative. The blood sugar was 84 mg. per hundred cubic centimeters, the urea nitrogen 12 mg. Sulfanilamide was not detected in the blood. Prostatic smear and culture yielded no specific organisms.

The patient gradually improved on bed rest, mild sedation and brewers' yeast. Muscle tenderness subsided and the knee jerks were elicited without reinforcement at the end of two weeks. The achilles tendon reflexes, however, were still absent. Sensory signs had completely disappeared but motor weakness was still evident, although so much improved that the patient became ambulatory the entire day without the use of a cane. Before further studies could be completed the patient again signed his release from the hospital, February 28, believing that he was almost cured.

#### COMMENT

Bliss and Long<sup>13</sup> have demonstrated that large doses of sulfanilamide administered to mice produced symptoms of bilateral vestibular dysfunction and a curious spastic paralysis. Hageman<sup>14</sup> obtained similar results in his experiments. Custer and his associates<sup>15</sup> have demonstrated the toxicity of the drug to

the central and peripheral nervous systems of dogs, producing ataxia, spastic paralysis, loss of reflexes and blindness. Hankins<sup>16</sup> has produced nervous symptoms resembling somewhat decerebrate rigidity in rabbits and cats with large doses of the drug. Bucy<sup>17</sup> has reported optic neuritis in man.

Marshall, Emerson and Cutting<sup>17</sup> believed that the occurrence and intensity of the toxic effects in man from sulfanilamide depended on the susceptibility of the patient to the drug, the dose per unit of body weight and the efficiency of the kidneys in excreting the drug. Unfortunately, our patient left the hospital before the renal function could be determined.

The possibility of gonorrhea as the etiologic agent in this case was considered, but in the past ten years there have been only two cases of gonorrheal neuritis reported in the literature, both in foreign journals.<sup>18</sup> It is probable, then, that sulfanilamide was responsible for the neuritic condition in this patient.

#### CONCLUSION

Toxic neuritis with a progressive muscular dystrophy-like picture probably resulted from excessive ingestion of sulfanilamide (2,000 grains [130 Gm.] in thirty-five days).

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#### HEMOPHILIA TREATED BY VENESECTION

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AND  
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J. E. M., a white man aged 51, was admitted to the Jefferson Hospital in March 1931, acutely ill with hemophilia. He presented signs and symptoms pointing to the presence of hemorrhage in the meninges, pleural cavities and abdominal viscera. There was bleeding from the genito-urinary tract, and there were also many large areas of subcutaneous hemorrhages.

After several days the patient was worse and in what seemed a hopeless condition; feeling that possibly these hemorrhagic crises were an effort of nature for relief, my associates and I tried venesection. The results were surprising. Though the patient had been in a comatose condition, forty-eight hours after the venesection he was clear mentally and seemed in good shape physically. Since that time, a period of seven years, he has been constantly under the care of one of us (A. B. G.) and has had venesection done, with the removal of about 500 cc. of blood, every six or eight weeks. With the onset of fullness in the head and pains in the joints he voluntarily comes in for venesection, and the relief of symptoms is almost always immediate. Since 1931, moreover, he has been free from subcutaneous hemorrhage.

Until about 1923 the patient had had frequent spontaneous bleedings from the nose and the roof of the mouth, with relief from the marked symptoms in the joints. From 1923 until he first entered the Jefferson Hospital in 1931, however, he had had no bleeding from the nose or mouth, and the symptoms in the joints were marked; he was confined in bed at times as long as six weeks. Frequently too he had had subcutaneous hemorrhages without apparent trauma. Of especial interest was the onset of these; at some point he would feel a slight stinging pain, and the next day a large area of discoloration would appear.

In October 1937 the patient was again admitted to the Jefferson Hospital for study. The frequent venesections since 1931 apparently had had no detrimental effects; for he seemed in good condition. But he had been suffering, he reported, a slight discomfort in one knee for some years.

When he was examined at this time his heart was normal, with a blood pressure of 150 systolic, 90 diastolic. There was only

16. Hawkins, Frank: Pharmacological Action of Sulfanilamide, *Lancet* 2: 1019 (Oct. 30) 1937.

17. Marshall, E. K.; Emerson, Kendall, Jr., and Cutting, W. C.: Para-Aminobenzenesulfonamide, *J. A. M. A.* 108: 953 (March 20) 1937.

18. Kunes, I.: Gonorrheal Polyneuritis, *Gyógyászat* 70: 344 (May) 1930. Kunes, Stephan: Gonorrheal Neuritis, *Deutsche Ztschr. f. Nervenheilk.* 121: 213, 1931.

1. Lawson, G. B.; Jackson, W. P., and Gardner, J. E.: A Case of Hemophilia Treated by Venesection, *J. A. M. A.* 98: 1443 (April 23) 1932.

13. Bliss, Eleanor A., and Long, P. H.: Para-Aminobenzenesulfonamide and Its Derivatives, *J. A. M. A.* 108: 32 (Jan. 2) 1937.

14. Hageman, P. O.: Toxicity of Sulfanilamide for Mice, *Proc. Soc. Exper. Biol. & Med.* 37: 119 (Oct.) 1937.

15. Custer, R. P., and his associates: *Proc. Philadelphia Path. Soc.*, March 10, 1938.

moderate peripheral arteriosclerosis. The electrocardiogram showed no essential abnormality. The hemoglobin content was 72 per cent (10.27 Gm.), the red blood cells numbered 4,130,000, the white blood cells 5,650: neutrophils 53 per cent, small lymphocytes 26 per cent, large lymphocytes 16 per cent, transitionals 2 per cent, eosinophils 5 per cent. The platelet count was 290,000, the clotting time, when a small test tube was used, was two hours and ten minutes, and the bleeding time forty-five seconds. The basal metabolic rate was plus 4. The clotting time, it seemed probable, had increased as the patient had grown older. Since his last visit to the hospital smaller amounts of blood have been removed because the hemoglobin content has been rather low. It is possible that the removal of smaller quantities is as beneficial as that of larger quantities.

During the patient's stay in the hospital in 1937 we had a woman with thrombopenic purpura who had been moribund. Transfusions had given her only temporary relief. Her blood and that of J. E. M. matched. With the hope of supplying some deficient element, we transfused 500 cc. of citrated blood into this woman's veins from the hemophiliac patient, but the response was about the same as what we had had with normal blood.

In studying J. E. M.'s history more carefully it was found that in 1929 he came to his physician (A. B. G.) and, because of the relief obtained by his previous severe spontaneous bleeding, demanded to be bled. This was at first refused but after insistence venesection was done with relief. This was repeated several times later. But we (Lawson, Jackson and Gardner) were not aware of this fact.

The family history of the patient is also most interesting. In addition to the uncles and brothers who were hemophiliac, he has one nephew aged 10 years (a sister's child) who has had bleeding from early childhood. When one of us (G. B. L.) saw him at the age of 3 he had a clotting time of two hours. Since then he has had many hemorrhagic crises, including an appendix operation (by Dr. J. C. Motley) in which much hemorrhage was found in the surrounding tissues. Dr. Graybeal, who was present at and advised this operation, is of the opinion that all the patient's symptoms were due to the hemorrhage. March 3, 1938, the boy was again seen by A. B. G. in an acutely grave condition. He had bleeding in the palmar surface of both forearms. His wrists were considerably swollen and could not be moved without intense pain. His fingers and entire hands showed extravasation of blood. There was a large hematoma on the left leg near the hip joint, with evidence of bleeding in the joint. There was also a large hematoma on the right leg around the hip joint with evidence of similar bleeding. So sore was the boy that he found it very painful to be moved in bed. His temperature was 102.6 F., pulse rate 126, white blood cell count 17,600; 275 cc. of blood was removed. In forty-eight hours the temperature, pulse rate and white blood cell count were normal, and the boy was sitting up in bed and did not complain of pain when any of his joints were moved. The clotting time of the blood was two hours and five minutes. Since that time the child has shown no evidence of recurrence of the bleeding and is now back in school and is leading a normal life.

Another patient (I. M. P.), a boy aged 15 years, and without a family history of bleeding, was sent to the Jefferson Hospital Jan. 19, 1938, by Dr. George Kolmer. Four days previously the boy had bitten his tongue slightly. Thereafter he began to complain of fullness in the mouth and tongue, though there was no evidence of sore throat. This fullness had increased with marked salivation but with very little soreness.

At the age of 2½ years he had marked spontaneous swelling in his joints, beginning in the right ankle. Since then this had continued at times, involving many joints. When he was 5 he suffered a minor laceration on the chin which, because of persistent bleeding, required hospitalization. At 7 years he had a retrobulbar hemorrhage causing the loss of vision in the left eye. When he was 12 a hordeolum of the left lid ruptured spontaneously, with bleeding so persistent that hospitalization was again necessary. In 1932 when one of us (G. B. L.) saw the boy he had a clotting time of thirty-seven minutes; two years later the clotting time was thirty-eight minutes.

Two weeks before I. M. P. was admitted to the hospital in January he had fallen from a pony and fractured his right fibula. There was marked swelling about the fracture. On examination the boy looked pale, except for his ears, which were pink. His mouth was partly open and his swollen tongue was visible. He opened his mouth with difficulty, the entire cavity being almost filled with the red swollen tongue. Under the tip was a gray slough. The floor of the mouth was markedly edematous, the edema extending to the right submaxillary angle and somewhat down into the right side of the neck. There was no light sense or pupillary reflex in the left eye. The lungs were normal. At the aortic area there was a slight systolic blow; the blood pressure was 120 systolic, 80 diastolic. The spleen was not palpable. The blood showed a hemoglobin content of 67 per cent (8.8 Gm.). The red cells numbered 2,700,000 and the white cells 9,900, with 70 per cent polymorphonuclear leukocytes. There were 346,000 platelets, and the clotting time was three hours and ten minutes. Venesection was done with the removal of 170 cc. of blood. The symptoms were markedly improved in twenty-four hours and the patient was soon able to leave the hospital. Two days after the venesection the clotting time was two hours and ten minutes.

#### COMMENT

In these venesections we have always used an aspirating needle in one of the veins of the arm, and there has been no subsequent bleeding at the point of insertion.

Our studies suggest that in hemophilia there are other factors in the hemorrhagic condition besides the delayed coagulation time, such as an increased volume of blood or more fragile capillaries, and it is possible that extravasation in the tissues may tend to increase hemorrhage.

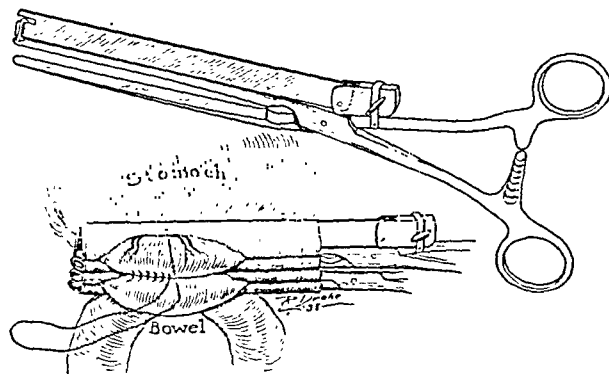
On each of the three patients studied here venesection as a therapeutic measure has been used at the time of a hemophiliac crisis. It has also been used for a number of years on one of these patients at the onset of symptoms. In every case the results have been remarkably good when the hemorrhage has been in the tissues, either with or without trauma. Whether it would be of value in cases in which there is a lacerated wound, such as occurs after a tooth is pulled or a finger is mashed, we are not yet ready to say.

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#### GASTRO-ENTEROSTOMY CLAMP

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The accompanying illustration of a modification of the older gastro-enterostomy clamp is more or less self explanatory. The purpose of the shelf is simply to hold the bulging stomach away



Gastro-enterostomy clamp.

from the line of suturing, thus aiding in the actual performance of the gastro-enterostomy. For his aid in the design credit goes to Mr. Richard Grounds, who always has been cooperative in matters of this kind.

From the Division of Surgery, the Mayo Clinic.

## Special Clinical Article

### ECZEMA AND ITS PRACTICAL MANAGEMENT

CLINICAL LECTURE AT SAN FRANCISCO SESSION

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AND

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The name eczema has for many years been applied to a heterogeneous group of inflammatory dermatoses. The vexed question as to what to include and what to omit from the broad concept of eczema is discussed in hundreds of articles, of which many are repetitive and many unproductive. In the curriculum of one of the postgraduate courses in dermatology the lecture on eczema deals with "eczema venenatum, seborrheicum, hemostaticum, infectious eczematoid dermatitis, neurodermatitis, dermatophytosis and dermatophytids." This classification, while recognizing different entities, adheres to the morphologic classification of widely differing dermatoses.

In recent years much has been added to our knowledge of the subject. Numerous useful and carefully organized facts have come to light and lines have been more sharply drawn. Unna long ago removed seborrheic eczema, better termed seborrheic dermatitis, from the general group and established it as a specific entity bearing no relationship to other members of the group. The eruptions caused by infection with fungi, such as eczematous ringworm of the hands and feet and the old eczema marginatum of Hebra, are now also eliminated and classified etiologically. Moreover, clinical investigations and studies in allergy have segregated infantile eczema and the neurodermites.

Eczema is not a disease entity. It is a reaction form which can be produced by contact of the superficial portion of the epidermis with a great many substances, some of which are primary irritants, and also by physical agents. Clinically eczema is characterized by erythema and vesiculation, at times by the formation of papules, and in the subacute and chronic stages by scaling, thickening and lichenification. The eruption is almost always accompanied by itching. Histologically eczema is characterized by spongiosis, vesiculation, acanthosis and parakeratosis of the epidermis and by edema, vascular dilatation and cellular infiltration, primarily perivascular, of the cutis.

The term eczema is restricted by some authorities to eruptions known or proved to be from hypersensitivity to contacts. While such limitation narrows considerably the number of dermatoses which can rightfully be called eczema, a great number still remain which fit into the eczema group morphologically but in which neither hypersensitivity to, nor contact with, any injurious agent can be proved. It has been suggested that the term eczematoid dermatitis may be used as a kind of "blanket indictment" to designate these various obscure members of the group, and—one might add—to cloak our ignorance respecting the fundamental causes of certain eruptions of the eczema family. This would add nothing to our understanding of the problem, since, as has often been pointed out, it would be illogical

to call an eruption eczema when the responsible agent is known and by another name when the etiologic agent has not been clearly determined or remains unknown.

#### PATHOGENESIS AND TESTING

A proper understanding of the pathogenesis of eczema is impossible without consideration of certain immunobiologic phenomena. The substances which provoke eczema in the sensitive person are often harmless to the normal person. The list of eczematogenous substances runs into the thousands, and with each new dye, each new chemical reagent and each new chemical substance introduced in industry another substance is added to the long list. R. L. Mayer has classified these substances under the following headings: (1) artificial manures, (2) cleaning materials, (3) oils, solvents and varnishes, (4) acids and alkalis, (5) aromatic oils, (6) alkaloids, (7) drugs of various composition, (8) soaps, (9) shoe creams and dyes, (10) paints and dyes, (11) disinfectants and (12) inorganic salts.

Many of these substances are primary irritants and, according to the duration of the contact, will produce erythematous, vesicular or necrotic reactions when applied to any skin. Others, for example certain mercury compounds, will produce eczematous eruptions in the normal person only if the concentration of the active agent is sufficiently high. In testing to demonstrate hypersensitivity it is therefore necessary to apply the allergen in a concentration which will not produce a reaction in the normal person but which will yet be sufficiently high to produce a reaction in the hypersensitive person. This optimum concentration has been worked out for a great many substances. For any new and suspected agent the concentration of the substance to be tested must be carefully determined.

#### TECHNIC OF TESTING

The eczematogenous (or suspected) substance is applied to a small area of normal skin, preferably on the forearm in adults and the back in infants; it is then covered with a piece of impermeable tissue, such as oiled silk or cellophane, which is somewhat larger than the area, and this is secured in place by adhesive plaster. (For persons sensitive to adhesive plaster frisket and similar substitutes are used.) When the substance to be tested is in liquid form it is applied by saturating blotting paper or a small square of linen with the solution. Many substances can be used in their natural state by moistening a small fragment of the material, such as shoe leather or clothing. The test substance is usually left in place for from twenty-four to forty-eight hours. If itching or smarting is present before that time the substance should be removed; these subjective sensations are indicative of a reaction and there is no added advantage in permitting further cutaneous irritation. Positive reactions range from mild erythema to the formation of bullae and even necrosis. Most common is the small vesicular or the small papular or follicular eruption, which is in essence only a limited reproduction of the eczematous process as it occurs naturally.

The outcome of the patch test is by no means always an exact reproduction of the eczematous process as it occurs on the patient's skin. This is especially true in industry. The patch test is only a temporary contact with a concentration which may be totally different from that with which the patient is employed; the test is applied to an area of normal skin which may or may not be hypersensitive and which has not previously been subjected to contact. Furthermore, such important factors as moisture, whether due to immersion of the hands or to perspiration, and injury to the skin caused by friction or heat and cold or in the form of cuts, burns or bruises, all of which favor the develop-

ment of sensitization, are not taken into account. The positivity or negativity of a reaction must therefore be critically evaluated. Whereas the positive reaction obtained with an eczematogenous agent with which the patient is employed usually leaves little room for doubt, the negative reaction alone is not a criterion for the exoneration of the allergen.

In industry, where one is dealing with known eczematogenous substances and where more than one person in factory or plant is usually affected, the offending agent is often easily determined. Outside of industry success in identifying the eczematogenous substance is not always a simple matter, and much depends on the patient's memory and intelligence as well as the physician's diligence. Frequently the time, the patience and the ingenuity of the physician will be taxed. Even after exhaustive search the cause may remain obscure until repeated contact leaves no doubt. There will be a large number of cases in which the cause cannot be determined and the condition is clinically eczema. Of these more will be said later.

Tests performed with a group of eczematogenous substances on eczematous patients are positive ten times as frequently as similar tests on noneczematous persons. The positive reactions obtained in the "normal" subjects may indicate that these persons are potentially eczematous and may acquire eczema after adequate clinical exposure. While sensitization may be monovalent, eczematous persons are usually polyvalently hypersensitive.

#### ALLERGIC ASPECTS

In eczema one is dealing with a condition which fits in with Pirquet's concept of allergy. The shock organ involved in this allergic reaction is primarily the epidermis, with the possibility that the upper part of the cutis also takes part in the reaction. The allergen may reach the epidermis by direct contact, as is most often the case, or via the circulation, by injection, by ingestion or by inhalation.

Is eczema in all instances based on allergy? An affirmative answer would require the assumption that the vesicular eruption produced by physical agents or primary irritants is not eczema; that the eruption caused by a 0.1 per cent mercury bichloride ointment in the hypersensitive person differs in its form from the eruption produced by a 50 per cent mercury bichloride ointment in the normal person. Such an assumption is neither warranted nor necessary. Eczema, as a specific reaction form, bears comparison with urticaria, another reaction form, also produced by numerous agents. Lewis has shown that urticaria resulting from an antigen-antibody reaction does not differ from urticaria caused by physical agents.<sup>1</sup>

There is no unanimity of opinion regarding the existence of antibodies in persons with eczema of hypersensitivity. Attempts at passive transfer by the Prausnitz-Küstner method, according to our experience, always give negative results. There are isolated reports, to be sure, of positive results of passive transfer tests. Some of these results were probably due to an associated urticarial hypersensitivity; others were obtained in patients with flexural neurodermatitis, a dermatosis which may simulate eczema clinically and with which circulating antibodies can frequently be

demonstrated. If antibodies exist at all in patients with eczema, they may be cell fixed, attached to the epidermis, and, if they are, one would hardly expect to be able to demonstrate them with a technic such as the Prausnitz-Küstner test. The Königstein-Urbach method of passive transfer, in which blister fluid is used instead of blood serum and antigen is applied by contact or by injection, was devised to demonstrate cell-fixed antibodies. Even with this method, passive transfer of sensitivity is not altogether successful. More information is needed on the subject of antibodies and eczema.

#### MECHANISM OF SENSITIZATION

The mechanism of sensitization is unknown. Eczema may make itself manifest after what is assumed to be a first contact, after exposure for a relatively short period (even a few minutes), after a few weeks of contact or only after years of contact, continued or intermittent. The reasons for the development of the sensitized state and the variation in the time between exposure to an eczematogenous substance and the development of the sensitized state (the refractory period) are unknown. Once developed, the sensitized state usually persists. It may, however, manifest itself only as a temporary phase, disappearing completely or recurring after repeated exposure. In some instances continued exposure creates a desensitized state which persists only as long as the person remains exposed to contact with the eczematogenous substance and disappears after temporary removal from the source of contact.

A high percentage of the workers employed in Japanese lacquer factories are victims of severe eczema. Continued exposure to the lacquer at first aggravates the eruption and then frequently produces a state of desensitization in which the worker is able to continue without fear of recurrence. Cessation from work may, however, be associated with a loss of this desensitization, with recurrence of the eruption on further exposure. Here, in one industry, is an example illustrating the various states of latency, incubation of sensitization, desensitization and loss of desensitization.

#### AUTOSENSITIZATION

The duration of the eruption following a single contact with an eczematogenous agent is relatively short. According to the severity of the eruption and the efficacy of treatment, the skin will return to normal in from seven to thirty days. Occasionally the eruption becomes more extensive, even generalized, and remains for a somewhat longer period but then goes on to complete healing. It may persist for a long time, even many years, new lesions appearing at previously unaffected sites while older lesions are undergoing healing. To explain the persistence of this eczematous process long after all contact with the original cause has ceased, the concept of autosensitization has been offered. The patient becomes sensitized to some product of his own damaged cells (an autogenous antigen). This concept is a most helpful one and offers a working basis for the explanation of many perplexing problems.

Concrete evidence in support of autosensitization are the reports of cases in which serum from eczematous patches in trickling over normal skin has produced linear areas of eczema confined to the site of contact. Contact with this serum did not produce eczema in normal persons. Absorption of this serum into the blood stream may produce eczema on other parts of the body. Whitfield attributed the widespread eczema

1. Macleod and Muende have suggested the possibility of the existence of an X substance in the epidermis, the release of which brings about the eczematous reaction. This hypothetical X substance evidently bears the same relationship to eczema that the H substance of Lewis bears to urticaria and serves to explain the occurrence of eczema, irrespective of the source, whether chemical or physical, allergic or nonallergic.



following irritation of a localized patch of eczema and the universal erythroderma and exfoliative dermatitis of psoriasis, and other noneczematous dermatoses following the vigorous application of topical remedies, to sensitization of the patient to his own tissue products.

#### MUTATION (?) OF CONTACT ECZEMA

We investigated a group of cases among which were cases of chronic generalized eczema and universal erythroderma. Some of the eruptions simulated dermatitis exfoliativa, pityriasis rubra of Hebra, mycosis fungoides, suspected Hodgkin's disease and leukemia implicating the skin. The routine contact tests in such cases are almost invariably negative. Nevertheless, we discovered, after long bouts of "third degree" questioning, that a considerable proportion of these chronic intractable eruptions began in the form of ordinary eczema affecting at first mostly the hands and forearms and often following industrial or occupational activities. In such cases, instead of the expected improvement or cure after cessation of occupational contacts or as a result of rational treatment, a steady and relentless progression of the eruption takes place, eventuating in a form of generalized or universal erythroderma. Clinically and often histologically the eruption has lost all semblance to the alleged contact eczema which preceded it. In some cases it is erroneously diagnosed as mycosis fungoides.

#### PREDISPOSITION

Is there an inherited predisposition toward the development of eczema? The eczematous type of hypersensitivity has been experimentally produced in both animal and man. Low produced a hypersensitive state in normal adults to the primrose plant by friction with the leaves. Bloch succeeded in sensitizing 100 per cent of human beings with primin, the crystalline active principle of the primrose plant. Eczematous sensitization has also been produced with other substances, including simple chemicals, both by contact and by injection. Despite these results, one is not wholly warranted in discounting an inborn predisposition, since, as has been pointed out, the ease with which sensitization is produced experimentally is in itself a variable factor.

Eczema developing after what appears to be a first contact with a given allergen would seem to favor the existence of an inherited or inborn—in contrast to an acquired—hypersensitivity. Actually it is difficult to prove that previous contact with that substance or some related product did not take place. Theoretically the possibility of sensitization by way of the placental circulation must also be considered, although there is no evidence for this in the case of eczematogenous allergens. On the whole the evidence at hand seems to negate the existence of an inherited hypersensitivity, but with all the gaps in the physician's knowledge, especially with regard to that large group of cases in which no etiologic agent is discovered, the existence of a dispositional hereditary factor in eczema must remain *sub judice*.

Of the traditionally listed predisposing causes of eczema, such as alcoholism, digestive disturbances, malnutrition, mental and nervous debility, endocrine disorders and errors of metabolism, we can, with due humility, say that almost nothing is known. To date there is little proof to warrant the acceptance of these factors as of special significance.

On the other hand, it is certain that infections, bacterial and mycotic, may predispose to the develop-

ment of sensitivity to other substances. The exact manner in which the sensitization threshold is lowered is unknown. Dermatophytosis as well as the deep mycoses produces a hypersensitive state which can be demonstrated by the intradermal reaction to the injection of trichophytin. Trichophytin, however, also produces an eczematous reaction on patch testing, and, since eczematous sensitization tends to polyvalence, the eczematogenous property of fungous products may serve to broaden the base of sensitization to include other agents. Moreover, sensitization to external allergens is facilitated by injury of the skin, in this instance injury produced by infection. Bacterial infection as a possible prelude to sensitization finds its best illustration in those cases of arsphenamine dermatitis in which sensitization appears to be based on a focus of infection.

It has previously been pointed out that sensitization may be localized. An occasional factor which seems to control this localization is previous damage to tissue. This damage may be the result of nutritional disturbances, as with varicose eczema; of previous inflammation from infection, as with ringworm infection, or even of inflammation from exposure to sun and wind.

One is led to conclude that the term allergic eczema must refer to eczema based on allergy in contradistinction to eczema in which allergy does not play a part. Unfortunately some authors use the term to designate an entirely different dermatosis which is also called disseminate neurodermatitis, pruritus with lichenification, exudative eczematoid and atopic dermatitis. While the condition was formerly classified with the eczema group there is at the present time little justification for continuing the use of a name for a disease which differs clinically and histologically from eczema and which by the use of the qualifying term allergic adds to the confusion.

#### THE INFANTILE ECZEMA-NEURODERMATITIS COMPLEX

Atopic dermatitis, or neurodermatitis, is a distinct disease entity. It is primarily a disease of youth, manifesting itself early in life, usually from the second to the fifth year, but it may appear at any time in life. It is a disease subject to spontaneous remissions and recurrences and is more prevalent during the fall and winter months. In New York and its vicinity a surprising number of patients return with a recurrence at the end of September or early in October, but to date no significant reason for this time relationship has been ascertained. While atopic dermatitis is common during the first two decades of life the incidence thereafter is much smaller and the intervals between attacks are longer.

#### CLINICAL ASPECTS

Atopic dermatitis favors the neck and flexures and attacks the antecubital and popliteal areas, the wrists (most often the dorsolateral aspects) and the face, especially the eyelids, forehead and upper lip, but often appears on other areas as well. In the very severe variety, which is fortunately the less frequent, the eruption may be universal. Clinically neurodermatitis is characterized by dry, scaly, scratched, thickened, lichenified and hyperpigmented areas with outlying small papular satellite lesions. Vesiculation is uncommon and is usually the result of irritation, chemical or mechanical. The eruption is accompanied by severe and sometimes maddening pruritus. Atopic dermatitis

of the scalp, except as an extension from the neck to the suboccipital region, is unusual. A common observation, however, is the diffusely scattered small blood crusted lesion resulting from excoriations with the comb and finger nails. We have not noticed this form of eruption in association with other dermatoses. Whenever it is present we feel that it is important in a differential diagnosis. A not infrequent part of the clinical picture is the dry, scaly, fissured and crusted eruption involving the dorsal aspects of the fingers and to a lesser degree the hands. In the absence of other features of neurodermatitis the true nature of the eruption in these locations is apt to be overlooked. In infants and children a widespread keratosis follicularis of the trunk is common.

In the majority of cases a family history of asthma, hay fever, infantile eczema or atopic dermatitis is obtained. The personal history may include asthma or hay fever or, if the patient is unfortunate enough, both of these. In over 60 per cent of the cases, infantile eczema appears to be a prodromal manifestation of disseminate neurodermatitis of childhood, adolescence and adult years. Like patients with asthma or hay fever but unlike those with eczema, patients with neurodermatitis in the majority of cases give immediate wheal and flare reactions to foods and inhalants on scratch or intradermal testing. The sensitivity is usually polyvalent. In almost all instances circulating antibodies can be demonstrated by the Prausnitz-Küstner test.

Not all eruptions clinically diagnosed as atopic dermatitis are associated with positive reactions to scratch tests. The differences between those which are and those which are not associated with positive reactions are subjects for further study. To differentiate atopic dermatitis further from the eczema group of diseases, hypersensitivity, as determined by the patch test, is no greater in the patient with atopic dermatitis than in normal persons. Nosologically atopic dermatitis belongs with the asthma-hay fever complex.

#### INFANTILE ECZEMA

Included in the comprehensive term infantile eczema are many of the vesicular, scaly and crusted itching eruptions of infancy. Clinically and histologically infantile eczema fits in with the adult form of eczema. However, certain characteristics of infantile eczema serve to differentiate it sharply from the adult form. Among the most important of these are the following: 1. A frequent familial history of asthma, hay fever, atopic dermatitis or infantile eczema is obtained. 2. Asthma or hay fever is common in later years in the children affected. 3. Wheal and flare reactions to tests with foods and inhalants are frequent. The unexplained reaction to egg white is especially common, its frequency according to some statistical data ranging as high as 90 per cent. Unfortunately the elimination of the substances to which positive reactions are obtained does not often bring about a cure of the eruption. 4. As the patient grows older the eczema has a pronounced tendency to disappear for a time, either wholly or partly, to be followed after varying periods by a morphologically and clinically different form of eruption, namely the disseminate form of neurodermatitis (atopic dermatitis).

Transition forms in which the clinical manifestations of neurodermatitis are present before healing of the eczema has taken place are not uncommon. The point to be stressed is that one is here concerned with

the early and late manifestations of one and the same dermatosis—the infantile eczema-neurodermatitis complex.

Not all forms of infantile eczema fall into the category of atopic dermatitis. Some are not based on atopy but are the result of irritation of young and tender skin caused by such substances as soap and wool or irritation due to an insufficient change of napkins. As compared with older children and adults, infants are not often subjected to contact with eczematogenous substances, and contact eczema is correspondingly uncommon. Seborrheic dermatitis of the scalp and face is, on the other hand, relatively common and if left untreated may go on to the development of a vesicular, crusted and impetiginized eruption sometimes clinically indistinguishable from the atopic form. Combinations of atopic and seborrheic forms seem to be common in infants.

#### TREATMENT

It is obvious from what has already been said about the multitudinous exciting or precipitating causes of eczema that scientific treatment must rest on the elimination of the cause. When that is possible there will in most cases be a spontaneous *restitutio ad integrum*. Symptomatic treatment is, however, essential in all cases, whether or not the cause has been determined, to secure relief of itching and burning and to hasten a return of the skin to normal. Even when the eczema is of undetermined origin, symptomatic treatment alone is sufficient to effect a cure in almost all cases, but the tendency to recurrence is relatively greater.

#### GENERAL TREATMENT

The patient with widespread or generalized eczema is a sick person. He needs rest in bed, the application of topical remedies by a competent nurse or orderly, the judicious administration of sedatives and the adjustment of splints or restraining devices to prevent scratching. He may require treatment by injections of various drugs or by roentgen therapy. Such treatment cannot be carried out when the patient is ambulatory and only with difficulty when he is confined to his home. He should be hospitalized to enable one to carry out procedures such as patch tests and various clinical and laboratory investigations. Hospitalization has the added advantage of removing him from his previous sources of contact, a measure which is sometimes helpful in determining the cause of contact eczema, especially when there are complications and the cause is obscure. Moreover, hospitalization considerably reduces the duration of illness and disability in the majority of cases.

The successful treatment of eczema is dependent on the relief of its most distressing symptom, pruritus. Pain in comparison is pleasurable, and it is this sensation which the patient substitutes in an orgy of scratching to relieve a crisis of itching. The cycle is a wicked one, for scratching aggravates the eczematous process, which in turn causes more pruritus. Listed hereafter, together with the various antieczematous remedies, are some of the more useful antipruritic drugs. It is necessary to call attention to the fact that drugs such as ethyl aminobenzoate, which relieve pruritus by their effect on the terminal nerve endings, are rather frequent sensitizers. Their effects must be closely watched. We are in the habit of performing patch tests and determining the patient's reaction to these substances before permitting him to use the prescribed remedy.

If necessary—and if the pruritus is at all pronounced it is necessary—rest and relief of itching must be

attained by the administration of sedatives. Bromides, barbiturates and salicylates will have to be tried. Opium and its derivatives are never to be used, no matter how severe the pruritus.

Paroxysms of itching may be so severe as to be uncontrollable by any known means, the patient scratching himself until his skin is lacerated and bleeding. On the other hand, itching may be slight and may often be readily controlled by topical applications. A properly adjusted, well padded splint on the upper extremities or a restraining jacket to prevent scratching and rubbing often proves to be a great aid in the control of subjective symptoms. At times even the lower extremities require splints. Once the patient has learned the value of restraining devices, he will actually demand their application during the night.

In general, baths, even baths medicated with starch, bran, oatmeal, potassium permanganate or tar, are

TABLE 1.—Remedies Used in Treatment of Eczema

*For Acute Eruptions*

Zinc oxide: zinc oxide ointment (U. S. P.); shake lotion; zinc-oil mixture  
Boric acid: boric acid ointment (U. S. P.); 3 per cent aqueous solution  
Solution of aluminum acetate (N. F.), or Burow's solution, diluted 1 to 10; Burow's paste  
Salicylic acid, 2 per cent solution; 2 to 4 per cent shake lotion or paste  
Resorcinol, 2 to 4 per cent solution  
Tannic acid, 2 to 5 per cent solution; 3 per cent shake lotion  
Silver nitrate, 0.125 to 0.25 per cent solution

*For Subacute Eruptions*

Ichthammol, 5 to 10 per cent shake lotion and ointment  
Solution of coal tar (N. F.), 5 to 10 per cent shake lotion and ointment  
Naftalan,\* 5 to 20 per cent ointment  
Crude coal tar, 0.5 to 4 per cent ointment  
Ammoniated mercury, 2 to 10 per cent ointment

*For Chronic Eruptions*

Oil of cade, 5 to 15 per cent ointment  
Oil of birch tar, 5 to 15 per cent ointment  
Crude coal tar, 5 to 20 per cent ointment; may also be painted on full strength  
Resorcinol, 4 to 10 per cent ointment  
Salicylic acid, 4 to 10 per cent ointment  
Sulfur, 4 to 10 per cent ointment  
Ammoniated mercury, 4 to 10 per cent ointment  
Chrysarobin, 0.5 to 10 per cent ointment

*Antipruritic Remedies*

Menthol, 0.25 to 1 per cent  
Phenol, 1 to 2 per cent  
Ethyl aminobenzoate, 3 to 10 per cent  
Solution of coal tar (N. F.), 3 to 15 per cent  
Ichthammol, 3 to 10 per cent  
Salicylic acid, 1 to 2 per cent  
Sulfur, 2 to 4 per cent  
Chloral hydrate, 2 to 4 per cent  
Spirit of camphor, 1 to 4 per cent

\* A distillate from Caucasian shale.

inadvisable in the case of acute and subacute eczema. We have time and again seen an existing eruption well on its way toward healing exacerbate after a single bath. On the other hand, in the case of dry, chronic, infiltrated eczema, medicated baths are of proved value and add much to the patient's comfort.

Except in the cases of eczema in which some specific food or foods is assumed to be at fault, diet plays a rather small part in the treatment. There are indications of the usefulness of dietetic restrictions in some cases, to be sure, and the future may hold much in store for patients who exhibit some error of metabolism, but at present the question of diet in the treatment of eczema is in a rather sad and chaotic state. Perutz, Gerson and others advise a low protein, high carbohydrate, moderately high fat regimen, with fruit juices and vegetables. When the condition is obstinate a salt-free diet deserves a trial.

While the literature is replete with reports of excellent results achieved with the intravenous administration of the various calcium salts; sodium thiosulfate, and strontium bromide in dextrose solution, our own experience with these drugs has been for the most part disappointing. Other nonspecific measures, such as the administration of the patient's own blood (autohemotherapy) and injections of turpentine and various forms of milk, have sometimes appeared to be effective, but it is difficult to judge the results since they were obtained in cases in which other forms of treatment were used in conjunction with these nonspecific measures.

Hyperpyrexia is another nonspecific measure which at times proves effective in the treatment of the widespread, generalized recurrent eruptions with a changing clinical picture in which one finds lesions of a different character, varying from the active exudative to the chronic lichenified type, in different stages of the disease. At one time the eruption takes on the appearance of universal erythroderma and at another it is indistinguishable from mycosis fungoides. For the production of heat various measures have been used, including cabinet baths (infra-red), diathermy (radiotherm) and typhoid vaccine. Recurrences of this type of eczema are nevertheless common.

Arsenic continues to hold an important position in the therapy of chronic eczema. It should never be used during the acute phase. In the subacute stage it is to be administered only if the eruption proves refractory to other therapeutic procedures. We prescribe solution of potassium arsenite in gradually ascending doses, starting with 3 minims (0.2 cc.) twice daily after meals and increasing the dose by 1 minim (0.6 cc.) daily until 20 minims (1.2 cc.) is taken. The dose can be maintained at this high level for several weeks. A course of arsenical treatment usually lasts from four to six weeks. Arsenical medication must not be frequently repeated, and the danger of delayed late effects, pigmentation, keratoses and epithelioma, must ever be kept in mind. At the first signs of intolerance, which include sweating of the palms, a coated tongue, dryness of the throat, abdominal pain and puffiness of the eyelids, the administration of arsenic should be discontinued. For subcutaneous administration sodium arsenate 2 Gm., phenol 2 Gm. and distilled water sufficient to make 100 cc. is used. This formula is also administered in gradually ascending doses starting with 3 minims once daily and increasing by 1 minim daily until a dose of from 20 to 25 minims (1.2 to 1.5 cc.) is reached, at which level it is maintained for a short time.

LOCAL TREATMENT

Thus far we have purposely refrained from any lengthy discussion of the morphologic characteristics of the various stages of eczema. They are too well known to bear repetition. In a discussion of the treatment, however, a consideration of the morphologic characteristics is of great importance, for the treatment is directly dependent on the clinical characteristics of the eruption. It is not a matter of indifference whether a salve, a lotion or a wet dressing is used in a given case. Each has its indications.

In table 1 are listed the most common remedies used in the treatment of eczema; as indicated, the remedies range from weak ones used for the acute eruptions to strong ones used for the chronic eruptions.

The number of remedies has purposely been limited. As in other branches of medicine, the intelligent and judicious use of a few well chosen remedies is wholly preferable to the haphazard use of many. To enhance

the effect of a lotion or salve a combination of two or more active ingredients is often preferable to an increase in the concentration of one active component.

If the choice of a remedy is important, the method of application is not less so. It does not suffice to prescribe a salve or a lotion and instruct the patient to "go home and use it." Remedies must be properly

TABLE 2.—Lotions and Pastes

1. Burow's Shake Lotion	
Burow's solution (solution of aluminum acetate N. F.)...	15.0
Zinc oxide	
Talcum .....	30.0
Glycerin .....	24.0
Solution of calcium hydroxide .....	120.0
2. Calamine Lotion	
Calamine .....	12.0
Zinc oxide .....	15.0
Glycerin .....	12.0
Solution of calcium hydroxide .....	15.0
Rose water .....	120.0
3. Bismuth-Oil Lotion	
Bismuth subnitrate .....	30.0
Zinc oxide .....	60.0
Olive oil .....	
Solution of calcium hydroxide .....	240.0
4. Zinc-Lime Water Lotion	
Zinc oxide .....	
Talcum .....	60.0
Glycerin .....	
Solution of calcium hydroxide .....	240.0
5. Zinc-Oil Mixture	
Zinc oxide .....	25.0
Talcum .....	25.0
Olive oil .....	50.0
6. Burow's Paste	
Burow's solution (solution of aluminum acetate N. F.)...	10.0
Wool fat .....	20.0
Lassar's paste .....	30.0

applied. Success in the hands of one physician and failure in the hands of another often depend on this factor alone. The patient should be instructed minutely in every detail; he should be advised (if this is indicated) to massage the salve into the affected area for several minutes by the clock, to apply a liberal layer, to cleanse the area with olive oil before each application and if possible to bandage the affected part. Wet dressings must be kept wet lest they serve as a source of irritation on becoming dry. Lotions are to be applied often and liberally, so that they thoroughly cover the affected area. Once daily the caked and crusted lotion should be removed by sopping the part with a 3 per cent aqueous solution of boric acid or with olive oil.

In the acute erythematous and vesicular stage, wet dressings are the treatment of choice. They are cooling, soothing and antipruritic, allow for drainage of serum, relieve swelling and give the patient more comfort than any other single remedy. Solution of boric acid 3 per cent, solution of aluminum acetate (N. F.) diluted 1 to 10, resorcinol 2 to 4 per cent, tannic acid 2 to 5 per cent, salicylic acid 2 per cent, are all effective and satisfactory. For impetiginized eczema, resorcinol 2 to 4 per cent, or 1:2,000 solution of mercury bichloride should be used for their bactericidal powers. Silver nitrate in a 1/8 to 1/4 per cent dilution is not sufficiently popular as a wet dressing. Were it not for the staining qualities which preclude its use on exposed portions of the body, silver nitrate would be the wet dressing of choice; it is to be highly recommended but must be employed with caution because of the possible development of argyrosis. Wet dressings should be bandaged whenever practicable and should be kept wet continuously until the dry, scaly stage is reached.

While lotions and pastes are not as effective as wet dressings during the acute stage, they are nevertheless satisfactory and in addition offer the patient a simpler and therefore often a more desirable form of treatment. They are prescribed when a wet dressing is not advisable.

The lotions and pastes listed in table 2 are recommended.

In the dry desquamative stage, treatment with a bland ointment such as boric acid (U. S. P.), zinc oxide ointment (U. S. P.) or Lassar's paste until the skin returns to normal, is indicated. Burow's paste, cooling, soothing and softening, may be helpful in the acute or in the dry desquamative stage.

The subacute stage, with its dry, crusted, scaly areas, is best treated with lotions or salves. We are rather partial to lotions, particularly for widespread eruptions. They offer a cleaner and more satisfactory form of treatment to the patient, are more easily applied and do not require bandaging. In subacute eczema the pathologic process is superficial enough to be influenced by the active ingredients in the lotions. The following substances are recommended: solution of coal tar (N. F.) 5 to 10 per cent, ichthammol 5 to 10 per cent, resorcinol 4 per cent, salicylic acid 2 to 5 per cent and tannic acid 3 per cent. These are to be added singly or in combination to the calamine lotion described. Burow's lotion may be used as a base instead of the calamine lotion for all the active ingredients except tannic acid. Tannic acid is incompatible and causes the mixture to cake. Ethyl aminobenzoate 5 to 10 per cent and menthol 1/8 to 1/4 per cent or other members of the antipruritic group should be added whenever necessary to control the pruritus.

The various active ingredients listed for subacute eruptions may be used in ointment form as in table 3.

Superficial, unfiltered roentgen rays in fractional doses are a useful adjuvant in the treatment of subacute eczema.

It is the dry, chronic, thickened, lichenified, scratched eczema which offers the most difficult problem and taxes

TABLE 3.—Ointments for Subacute Eruptions

Ethyl aminobenzoate .....	5.0
Naftalan .....	3.0-10.0
Salicylic acid .....	2.0
Zinc oxide .....	
Starch .....	25.0
Yellow petrolatum .....	100.0
Menthol .....	0.15
Solution of coal tar (N. F.) .....	3.0-6.0
Solution of aluminum acetate (N. F.) .....	10.0
Wool fat .....	20.0
Lassar's paste .....	60.0

TABLE 4—Coal Tar and Salicylic Acid

Crude coal tar .....	4-10%
Salicylic acid .....	4-10%
Hydrous wool fat .....	
Petrolatum aa q. s.	

the skill of the physician. The remedies employed are all reducing agents, and of these tar is outstanding. It is the most important and reliable single therapeutic agent used in the treatment of chronic eczema. Salicylic acid 3 to 10 per cent and resorcinol 4 to 10 per cent added to the preparation promote the effects of the tar by their keratolytic action.

Fractional doses of roentgen rays are most helpful in the treatment of chronic eczema in which the skin is

lichenified and thickened, especially when it is localized. Frequently the use of roentgen rays is the only satisfactory form of treatment and patches which have resisted topical remedies of all kinds will yield to four or five weekly exposures. In cases of recurrent eczema overdoses must be guarded against and roentgen therapy must be stopped when the limit of tolerance is reached.

Certain regional eczemas require special consideration. In the case of acute vesicular dermatitis of the extremities accompanied by swelling and tension, elevation of the extremity, upper or lower, by improving circulatory dynamics will hasten a return to normal.

TABLE 5.—Zinc-Gelatin Formula

Mixed zinc oxide and calamine.....	30.0
Gelatin .....	30.0-40.0
Glycerin .....	50.0
Water .....	ad 200.0

The course is otherwise often a protracted one. In the case of subacute and chronic eczemas of the extremities, especially the lower, the application of Unna's zinc-gelatin boot will bring relief to the patient and will promote quicker healing than any other measure we can recommend. We encase the extremity in a stockinet bandage, apply the warmed, liquid zinc-gelatin mixture directly to the stockinet and then bandage the extremity firmly with an ordinary gauze bandage. We find this method superior to the application of the zinc-gelatin mixture directly to the skin followed by cotton wadding or the tedious application of the mixture directly to the bandage in its endless circuitous course. Bandages already impregnated with a gelatinous material which dries readily and which form an excellent boot are now on the market.

There are various modifications of Unna's original zinc-gelatin formul , all satisfactory. Proprietary preparations are also available.

The application of the bandage may be preceded by the application to the lesions of tar ointment or gentian violet 2 per cent in 50 per cent alcohol. The gentian violet is useful in the treatment of the nummular, vesicular, crusting patches so often found on the extremities.

Ecze ma of the axillary, pubic and crural regions is best treated with shake lotions such as calamine lotion with the addition of antipruritics and active agents such as solution of coal tar (N. F.) 3 to 10 per cent and resorcinol 2 to 4 per cent. Salves in these areas lead to annoying folliculitis.

The eyelids must be treated gently. Wet dressings of boric acid solution or solution of aluminum acetate (N. F.) diluted 1 to 15 are usually helpful. The patient must be in a reclining position, and the wet dressings should be applied for several hours daily. In the acutely erythematous, edematous stage, continuous application of wet dressings for from twenty-four to seventy-two hours gives the greatest amount of relief and brings about the most improvement. In the dry, scaly stage, boric acid ointment or the 1 per cent yellow mercuric oxide ophthalmic ointment is satisfactory. Boric acid ointment should also be applied in the intervals between wet dressings. Roentgen rays in small fractional doses are sometimes necessary to control the process.

INFANTILE ECZEMA

The subject of infantile eczema forms too large a chapter for lengthy discussion in this communication. Only the more important measures will be indicated.

In the first place the infant is to be kept at rest with the extremities tied to the sides of the crib or splinted to prevent scratching and irritation. Errors in diet, such as overfeeding in the case of the obese child and insufficient feeding in the case of the poorly nourished child, must be corrected. Idiosyncrasy to milk or some other article of food in the infant's diet is often at fault. Elimination of the food product in question, boiling of the milk, addition of hydrochloric acid and substitution of a soybean preparation for milk are all helpful measures which can be tried. If possible the diet should be arranged by consultation with a pediatrician.

Locally, White's crude coal tar ointment<sup>2</sup> offers excellent results in the treatment of infantile eczema. The tar and zinc oxide are each separately mixed, as are the starch and petrolatum, and then these two combinations are thoroughly mixed. If a distilled crude coal tar product is used the folliculitis which commonly follows the use of ordinary crude coal tar will often be prevented. The salve should be thoroughly applied to the face and scalp and then covered with a mask. Not all eruptions require such diligent treatment. The remedy should be tempered to the clinical condition, and a mild infantile eczema will often yield to treatment with 10 per cent naftalan in zinc oxide ointment. The eruption on the body, if present, is not as infiltrated and requires milder remedies, such as 1 to 2 per cent of oil of birch tar in zinc oxide ointment, 5 per cent naftalan ointment or a shake lotion.

It might be well to repeat that the treatment of eczema in its various and diversified forms and aspects requires meticulous attention to detail on the part of the physician and whole hearted cooperation on the part of the patient.

TREATMENT OF ATOPIC DERMATITIS

The logical treatment of a constitutional disease such as the infantile eczema-atopic dermatitis complex should naturally be directed to the constitutional basis on which the disease depends. Unfortunately little can be done to influence the atopic state. The immunologic approach serves as a basis for comprehension but is of little practical therapeutic value. Neither the elimination of

TABLE 6.—Ointment and Lotion for Pruritus

Menthol .....	0.15
Phenol .....	0.6
Naftalan .....	6.0
Zinc oxide oint. ....	q. s. 60.0
Menthol .....	0.3-0.6
Phenol .....	2.4
Ethyl aminobenzoate .....	12.0
Solution of coal tar (N. F.) .....	12.0
Lotion of calamine and zinc .....	q. s. 240.0

Sig.: Shake thoroughly and paint on liberally with a brush from three to ten times daily.

the specific allergens to which the patient gives test reactions nor specific hyposensitization is frequently successful. There are isolated instances, to be sure, in which the elimination of food or environmental allergens appears to be beneficial, and it is the good results in these cases which warrant testing, elimination and hyposensitization; nevertheless these results are more exceptional than usual. From a practical point of view reliance has to be placed on topical remedies and symptomatic and general measures. These give the most satisfactory results.

2. Crude coal tar 2 Gm., pulverized zinc oxide 8 Gm., starch 8 Gm. and sufficient petrolatum to make 30 Gm.

In the general treatment of atopic dermatitis, mental and physical rest is essential. Almost invariably the person with neurodermatitis is highly strung, ambitious, alert, overactive and highly emotional. These characteristics are already evidenced in the precocious, restless infant, in constant motion during the entire consultation. Not infrequently the attack is precipitated by some unusual strain and in youngsters often occurs just prior to or during examination periods. Whatever the immediate cause, it is essential to regulate the patient's life, remove all sources of irritation and advise sufficient rest. This is not a simple matter, as any one who has had to deal with this problem will readily acknowledge. In one instance a sufficient amount of rest may mean retiring two hours earlier, in another enforced afternoon rest periods may be required and in still others hospitalization is necessary.

Rest is abetted by the administration of sedatives, and there need be no great hesitancy in adopting this measure unless there is a history of hypersensitiveness. Bromides and barbiturates (especially phenobarbital) are valuable. Intravenous bromotherapy (strontium bromide) is used, but its superior qualities are questionable. Sedation is a necessary part of the treatment and is used not only to lower the threshold of irritability but also to allay the uncontrollable pruritus from which the patient suffers. Treatment directed to the imbalance of the autonomic nervous system is not sufficient unto itself, but as part of a scheme in which other forms of treatment are used, atropine, pilocarpine and ephedrine find a place.

Without pruritus there would be no neurodermatitis, and local treatment is based on the one essential point of controlling pruritus. Lotions and ointments are equally valuable, but only trial and error can tell which is the more suitable for the individual patient. Ointments often seem to give more relief and more comfort. Their use can be combined, the more cleanly lotion being used in the daytime and the ointment at night. Usually the simpler the treatment the better it is. The preparations in table 6 are suggested.

The ointment can be fortified by the addition of ethyl aminobenzoate for its antipruritic action, and instead of naftalan other tar preparations such as carboneol<sup>3</sup> (3 to 6 per cent), oil of birch tar (5 to 10 per cent) and crude coal tar (5 per cent) may be substituted or added in combinations. As a rule these are satisfactory, and if they are not it is doubtful that any other topical remedies will be more beneficial. If the lesions have become impetiginized, from 3 to 5 per cent ammoniated mercury should be added to the ointment. Ointments must be gently massaged in for several minutes; a liberal layer must be left over the affected area, which is then properly bandaged. We have found bandages rather irritant and have used stockinets on the extremities with satisfaction. In cases of severe and extensive involvement proper treatment cannot be carried out without the help of trained personnel and hospitalization.

Bathing is not contraindicated. With a widespread eruption it is distinctly beneficial and sometimes gives more relief than any other single remedy. The warm colloid bath prepared with starch, bran or oatmeal is preferred; it should last for from twenty to thirty minutes but may be much more prolonged if beneficial.

Of the many other remedies used, arsenic and calcium, especially the former, are the most useful. The fact that neurodermatitis is a recurrent disease and that

courses of arsenic cannot be repeated indefinitely must not be lost sight of. Solution of potassium arsenite in the usual dose is administered by mouth unless gastric irritation necessitates a change to subcutaneous administration, when the 2 per cent solution of sodium arsenate is preferred.

Roentgen therapy is the most powerful antipruritic. As such it forms a most important part of the therapy of atopic dermatitis, but the problem of roentgen therapy is one with many facets and its use should be confined to the specialist.

200 West Fifty-Ninth Street.

## Special Article

### THE PHARMACOPEIA AND THE PHYSICIAN

#### THE TREATMENT OF INFANTILE ECZEMA

FROM THE POINT OF VIEW OF THE PEDIATRICIAN

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BOSTON

*This is one of a series of articles written by eminent authorities for the purpose of extending information concerning the official medicines. The twenty-four articles in this series have been planned and developed through the cooperation of the U. S. Pharmacopoeial Committee on Revision and THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.—ED.*

In order to discuss treatment intelligently, it is first necessary to indicate briefly what is meant by "infantile eczema."

It would be not only futile but presumptuous for a pediatrician to attempt a definition of the word "eczema" when dermatologists have been trying for years to formulate one that would be satisfactory to every one and have not yet succeeded. Suffice it to say that there is in infancy a certain group of dermatoses which is perhaps best called the "eczematoid" group, and that the dermatoses included in it present certain morphologic and clinical characteristics which set them apart from other dermatoses. The component elements of the group are the seborrheic, the atopic, the contact and the mycotic forms of dermatitis.<sup>1</sup> Added to any one of these may be the elements of traumatic or chemical irritation or of pyogenic infection. Combined forms are frequent, and the morphology is so variable that it is often not possible to classify a given case accurately. The last two members of the group, contact and mycotic dermatitis, while they do occur in infancy, are not common and will not be discussed.

Most "eczemas" of infancy are of the seborrheic or atopic variety, and combinations of the two are common.

Seborrheic dermatitis occurs especially in fat babies during the early months of life. It is likely to begin with intertrigo of the folds and greasy scaling of the scalp ("cradle cap"). It may then extend to other parts of the body, most often the face, neck, shoulders and trunk. It is essentially a dry, scaly eruption and rarely oozes unless there has been rubbing. On the body the patches of dermatitis, usually with sharply

3. A product of crude coal tar dissolved in carbon tetrachloride.

This is the first of three articles on this subject.  
1. Sulzberger, M. B.: J. Michigan M. Soc. 34: 78 (Feb.) 1935.



defined margins, may be large or small, round or oval, often a yellowish pink and with a tendency to clear in the center. By fusion of several patches, large sheetlike areas are sometimes formed. The scales may be silvery white and dry, somewhat suggesting those of psoriasis, but more often they are yellowish and greasy. There is sometimes a tendency to erythroderma, typically seen in Leiner's disease (erythrodermia desquamativa), which is regarded as the most severe type of seborrheic dermatitis. Leiner's disease is uncommon in this country.

There is only moderate itching, or sometimes none, and in an uncomplicated case protein tests on the skin are negative. The etiology is not settled, and a discussion of the various theories of etiology would be out of place here. There is no evidence to indicate that seborrheic dermatitis is of allergic origin; and it is not associated with asthma or hay fever. Permanent recovery after a few weeks or months is the rule.

Atopic dermatitis is the most common form of "eczema" in infancy. By the word "atopy," suggested by Dr. Arthur Coca in 1922, is meant a special and particular form of allergy in which there is a disposition, often determined by heredity, to a pathologic sensitization with foreign protein or protein-like substances and manifested particularly by the development of dermatitis, asthma or hay fever.

Atopic dermatitis in the infant is the commonest early expression of atopy. The eruption usually begins on the cheeks and is often preceded by seborrheic manifestations on the scalp. It may be confined to the head but more commonly spreads to the arms, legs and trunk, or it may become generalized, so that it covers most of the surface of the skin. The clinical appearance is variable: erythema, macules, papules, vesicles, scales, crusts and even wheals may exist all together. Added to these may be pyogenic infection and excoriations caused by scratching. The most characteristic elementary lesion, if one can speak of an elementary lesion in a dermatosis with such a varied morphology, is a small exudative papule which often goes on to frank vesiculation. These exudative lesions may rupture or may have their tops removed by scratching, with resultant formation of a small crust, so that there is often a punctate appearance which some have thought is quite characteristic of atopic dermatitis. Since vesiculation is often a prominent feature, in contrast to seborrheic dermatitis, oozing is common. Sometimes there may be rather large, somewhat thickened, fairly sharply defined areas made up of many small papulovesicles. In general, sharp margins are not characteristic of the eruption of atopic dermatitis.

The itching is intense; there is no dermatitis that itches more. Protein tests on the skin are often positive, the blood may contain transferable antibodies (reagins) and there is usually an eosinophilia. Some infants recover entirely after the end of the first year. All too commonly, however, the condition persists, either continuously or with remissions and exacerbations, well into childhood or even into adult life, and asthma or hay fever may become associated with it.

#### RELATIONSHIP OF ATOPIC TO SEBORRHEIC DERMATITIS

Modern dermatology has been able to separate the "seborrheic eczema" of the adult, which Unna first described in 1887, from true eczema. The distinction is more difficult in infancy. There are many cleancut cases that can be accurately and unequivocally assigned

to one group or the other, but seborrheic manifestations so frequently in young infants precede the development of true atopic dermatitis before any allergy has apparently developed, and mixed forms are so common, that there is evidently some relationship between the two. What this relationship is is by no means clear, and it would not be desirable in a practical paper of this sort to embark on a theoretical discussion. It is likely, however, that in the mixed forms the cutaneous symptoms are not entirely dependent on the antigen-antibody reaction of atopy and that there are other unknown etiologic factors.

#### LOCAL TREATMENT

There have been innumerable preparations recommended, many of which accomplish but little. I shall mention only the few that I have found the most reliable.

1. *Seborrheic Dermatitis*.—The Scalp: Prescription 1 is typical of those found valuable on the scalp. This ointment is applied heavily and is well rubbed in each day for four days; the scalp is then covered with a

#### PRESCRIPTION 1.—Salicylic Acid Ointment

	Gm. or Oz.
Salicylic acid .....	2
Petrolatum .....	129

Mix and make into an ointment.

cheap cotton cap. On the fifth day it is shampooed with soap and water, and the loosened scales are scraped off with a fine comb. This course of treatment is repeated as often as necessary. Good results should be obtained. As a rule scalps are not very hard to deal with.

The Face: Treatment of the face is more difficult because it is continually exposed and it is never possible to avoid a certain amount of rubbing. In my experience, for treatment of the face a paste made from crude coal tar, originally suggested by Dr. Charles J. White is excellent (prescription 2).

#### PRESCRIPTION 2.—Coal Tar Paste for the Face

	Gm. or Oz.
Coal tar, N. F. ....	7.5
Zinc oxide .....	15.0
Starch .....	30.0
Petrolatum .....	120.0

Mix and make into an ointment.

This is applied as often as is necessary to keep the face covered. It should not be used if pyogenic infection is present. After the tar paste has been used for about a week there should be marked improvement, but it is well to keep on using it until the skin is somewhat wrinkled and drawn. At this stage it is discontinued, and an ointment composed of equal parts of compound ointment of resorcinol (N. F.) and cold cream (rose

#### PRESCRIPTION 3.—Coal Tar Ointment for the Body

	Gm. or Oz.
Coal tar, N. F. ....	7.5
Petrolatum .....	60.0
Wool fat .....	60.0

Mix and make into an ointment.

water ointment, U. S. P.) is applied. This is continued as long as there is any appreciable dermatitis present. When the cheeks have reached a stage at which they are perhaps a little too red, with a tendency to chapping, but with no severe dermatitis, cold cream (U. S. P.) is substituted for the compound ointment of resorcinol and is continued indefinitely. If in the beginning the dermatitis is mild, it may not be neces-

sary to use the paste of crude coal tar, and good results are often obtained with one of the proprietary ointments of white tar (Ultraine, Taralba, Supertah).

The Body: For large areas on the body, a somewhat different tar ointment, without the zinc oxide and starch, is used (prescription 3). The entire trunk should never be covered with tar ointment or paste, since tar may be toxic if absorbed in too great quantity.

**PRESCRIPTION 4.—Undiluted Crude Coal Tar**

Coal tar, N. F. .... 30 cc.

**PRESCRIPTION 5.—Plain Talc for Intertrigo**

Purified talc ..... 120 Gm.

An ointment is not so satisfactory if there are only a few coin-size patches. For these, crude coal tar undiluted is painted on once a day with a cotton swab (prescription 4).

Intertrigo: For the intertrigo that is so often present, a dry dusting powder is better than an ointment. None is better than plain talc (prescription 5).

2. *Atopic Dermatitis.*—The Scalp: The same treatment is recommended as for seborrheic dermatitis.

The Face: If only a moderate amount of oozing is present, tar paste may be applied at once and is followed by compound ointment of resorcinol the same as for seborrheic dermatitis. If there is much weeping, this must be controlled before any ointment or paste is applied. It is not desirable to use a lotion which contains much sediment; there is too much caking. Liquid applications that have the active medicament in solution are the best. I have found prescription 6, originally suggested by Dr. Schlotz of Los Angeles, very efficient.

**PRESCRIPTION 6.—Lotion for Atopic Dermatitis of the Face**

	Gm. or Cc.
Solution of lead subacetate .....	15
Solution of aluminum subacetate .....	15
Distilled water .....	enough to make 120

Mix and make into a lotion.

**PRESCRIPTION 7.—Lotion for Atopic Dermatitis of the Body**

	Gm. or Cc.
Liquefied phenol .....	4.0
Solution of coal tar .....	15.0
Calamine lotion .....	enough to make 120.0

Mix and make into a lotion.

A saturated aqueous solution of boric acid is also good and is best if there is any tendency to infection.

Either of these is sopped on every hour until the oozing is controlled, which usually takes about three

**PRESCRIPTION 8.—Boric Acid or Salicylic Acid**

	Gm. or Cc.
Boric acid ointment .....	120

**PRESCRIPTION 9.—For Pyogenic Infection**

	Gm. or Cc.
If Oozy	
Solution of potassium permanganate (1:2,000) .....	240
Mix and label Apply frequently	
or	
Solution of boric acid, N. F. ....	240
Mix and label Apply frequently	
If Not Oozy	
Ammoniated mercury ointment (5 per cent) .....	120

days. Tar paste is then applied. The same principles apply to oozing on any other part of the body.

The Arms and Legs: These are treated in the same way as the face, with the exception that they should be bandaged. One layer of ordinary bandage is not enough; it is well to apply an outer elastic bandage also.

The Body: If there is an eruption of small macules or papules all over the trunk, dry powdering with talc is probably better than the use of an ointment or a lotion. If there are irregular areas of grouped papules and vesicles, prescription 7 may be used.

Erythroderma: If there is diffuse redness with scaling all over the body (atopic erythroderma), as there may be in some of the worst cases, strong ointments or lotions should not be used. Although there is no local treatment that is very efficient for this symptom complex, it has seemed to me that frequent powdering with talc is as good as anything. If this is too drying and an ointment seems indicated, either prescription 1, 8 or 9 will do no harm and may do some good.

**CONTROL OF ITCHING**

I know of no local application that is really satisfactory to control itching: the itching is too widespread. Five grains (0.3 Gm.) of phenol added to an ounce of

**PRESCRIPTION 10.—Sedative to Control Itching**

	Gm. or Cc.
Phenobarbital .....	0.2
Lactose .....	1.3

Mix and make into twelve powders.

ointment or lotion is probably as good as anything, but if the baby sleeps poorly at night an internal sedative is better (prescription 10).

**DIETETIC TREATMENT**

Some eczematoid eruptions (mycotic and contact) have nothing to do with the diet. This should be remembered by pediatricians particularly, for they have perhaps been too ready to believe that any and all cutaneous eruptions in infancy are of dietetic origin. Dietetic therapy is, however, often of value in seborrheic and in atopic dermatitis.

1. *Seborrheic Dermatitis.*—Since there is no specific food sensitization in uncomplicated seborrheic dermatitis, there is no indication for the omission of any particular food. Many infants with seborrheic dermatitis and intertrigo are too fat, and moderate underfeeding often has a favorable effect. It has also been

**PRESCRIPTION 11.—Feeding Low in Fat and High in Protein**

2 per cent milk .....	26 ounces
Water .....	9 ounces
Karo corn syrup .....	2 tablespoonfuls
Powdered casein .....	4 level tablespoonfuls

found that they are likely to do best on a formula which is relatively low in fat and high in protein. Such a formula for a 4 months old infant is given in prescription 11. Other than this they should be fed as any baby is fed.

2. *Atopic Dermatitis.*—Just as innumerable preparations have been used in the local treatment of atopic dermatitis, so have many methods of diet been recommended, most of which have enjoyed a brief popularity and have then subsided. At the present time, dietetic treatment in accordance with the immunologic observations is accepted by most pediatricians; and, while by no means entirely satisfactory, is undoubtedly superior to any other that has ever been recommended.

The theory most widely held is that the eruption is produced by a histamine-like substance which is either newly elaborated or set free by the union of the antigen or antigens to which the individual is hypersensitive,

with specific antibodies that are fixed in the papillary layer of the cutis. (See the publications of Marion B. Sulzberger.) In accordance with this theory the commonly accepted immunologic treatment is to determine by means of the cutaneous tests, history and clinical trial the antigen or antigens to which the patient is hypersensitive and to withdraw these from the diet or environment. Hyposensitization, while it may be occasionally useful, does not hold the important place in atopic dermatitis that it does in hay fever. In infancy, the food allergens are by far the most important, although there may sometimes be sensitization to environmental allergens, and these must be taken into consideration.

THE CUTANEOUS TESTS

It is often not possible to make sure by inspection alone whether an eruption is of the atopic variety. It is therefore desirable to do cutaneous tests on all infants with eczematoid eruptions, no matter what the structure. While testing of the skin is not always reliable and has many pitfalls and disappointments, it has revealed more about the essential nature of atopic dermatitis than has anything else, and has offered the best indications for etiologic treatment that have yet been available.

Positive Scratch Reactions to Foods in 100 Atopic Infants Under 1 Year of Age, All of Whom Reacted to One or More Allergens

Egg white .....	86	Rice .....	2
Milk .....	26	Corn .....	2
Wheat .....	17	Spinach .....	2
Oat .....	8	Pea .....	2
Barley .....	6	Carrot .....	2
Beef .....	6	Orange .....	2
Potato .....	4	Codfish .....	1
Haddock .....	3	Chicken .....	1
Tomato .....	3		

Three methods of testing are employed:<sup>2</sup> (1) the scratch test, (2) the intracutaneous test and (3) indirect testing (passive transfer). With infants the scratch test is preferable as a routine, but if it is negative it should be followed by an intracutaneous test with certain of the more important allergens. Indirect testing is somewhat cumbersome and complicated for average use but it is the only method that can be employed when the entire surface of the skin is covered with dermatitis.

*Allergens with Which to Test.*—It is not necessary to test young infants with a large number of allergens; tests should be made with the few foods they are eating, plus egg white whether they are eating it or not and with a few of the more important environmental allergens to which they may have been exposed. A positive test does not indicate with certainty that the dermatitis is due to the allergen in question; it indicates a possible etiologic factor only. If the positive test, however, is consistent with the history, it should be considered of etiologic significance until proved otherwise. The reactions to the scratch test by 100 infants are given in the accompanying table.

*Egg White:* Most atopic infants react to egg white although most of them have never eaten it. The sensitization is probably of intra-uterine origin (Ratner). In spite of frequent positive reactions, egg is

of but little practical importance as a causative factor in the atopic dermatitis of young infants, since most of them have never eaten it, and those who have have had it removed from the diet as soon as the dermatitis started, usually without any benefit whatever. A positive reaction to egg is of some diagnostic importance, however, since it usually indicates that the infant is atopic.

*Milk:*<sup>3</sup> Sensitivity to the proteins of cow's milk is probably the most important single cause of atopic dermatitis in infancy. As the intracutaneous test with milk is often positive when the scratch test is negative, it should always be done after a negative scratch test. A positive scratch test almost always indicates clinical sensitivity; a positive intracutaneous test sometimes does. In the presence of sensitivity to milk, one of the three diets may be used: (1) evaporated cow's milk, (2) goat's milk, either fresh or evaporated, (3) entire withdrawal of milk, and the substitution of a milk-free food, of which there are several on the market.

In my experience, evaporated cow's milk is not often very efficacious but is the best form of milk if cow's milk is to be used at all. Goat's milk is very uncertain but may occasionally give brilliant results. Withdrawal of milk and the substitution of a milk-free food give more consistent results, and I have had by and large better results with this in atopic eczematous infants than with any other form of dietetic therapy. It does not always work, however, for sensitivity to milk is by no means always the cause of atopic dermatitis, although it is in infants the most common one. Furthermore, in "atopic erythroderma," in which there is diffuse redness of the entire body, a great deal of coarse scaling and a general glandular enlargement, a milk-free diet is not often successful in spite of the fact that most of these infants are sensitive to milk. Nor should the milk-free foods be used in undernourished infants or in those with a tendency to diarrhea, for they may not be well tolerated by such infants, and a diarrhea may arise which may be more serious than the original dermatitis.

*Cereals:* Sensitivity to cereals, especially wheat, is common but offers no great difficulty, as there are so many to choose from.

*Vegetables:* Sensitivity to vegetables, especially peas and spinach, occasionally occurs but is rarely the most important or primary cause of the dermatitis.

*Orange Juice:* Scratch tests with orange are rarely positive; the intracutaneous test is occasionally positive. Sometimes, in spite of negative tests, the mother is certain that after the infant takes orange juice there is increased itching or an exacerbation of the eruption. Ascorbic acid is easily substituted.

*Fish Oil:* This may occasionally be a cause of atopic dermatitis—there is no evidence to indicate that it is commonly so. It should not be omitted from the diet unless a cutaneous test with fish has been done and is positive.

While it is more accurate to be guided by the results of cutaneous tests in planning a diet, it is possible, by knowing what foods most frequently cause trouble in the majority of atopic infants, to construct a diet which will come fairly close to meeting the immunologic indications even if cutaneous tests are not done.

2. For the details of testing of the skin see any of the textbooks on allergy.  
3. For a more complete discussion of this important subject than is possible here, see Brennemann, Joseph: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1938, chapter 43, vol. IV.

Such a diet is as follows:

Evaporated cow's milk or goat's milk for mild cases or for any infant whose nutrition is poor

A milk-free food for moderately severe or severe cases if the nutrition is good

Cornmeal or oatmeal

Carrots or string beans

Banana

Fish oil

Ascorbic acid

#### NONSPECIFIC REGULATION OF THE DIET

Any digestive disturbance may aggravate atopic dermatitis; if there is a tendency to loose stools, constipation or vomiting, this should be corrected. If the baby is too thin he should be made fatter; if he is too fat he should be made thinner. If he has been taking too large an amount of milk, which is often the case, this should be reduced, or if he has been getting milk from a Jersey or a Guernsey herd his milk supply should be changed to one that contains less fat. There is rarely any advantage in changing from one sugar to another.

*Importance of an Adequate Diet.*—No matter what the cutaneous tests show, no changes in diet should be made which might jeopardize the general health of the infant: the whole child is more important than his skin, and an adequate diet on which he can thrive must be supplied at all times.

#### ENVIRONMENTAL ALLERGENS

Many eczematous infants have specific cutaneous hypersensitivity to house dust and feathers. It is difficult to prove that this has anything to do with the eczema, but it is well to allow no atopic eczematous infant to sleep on a feather pillow and to keep his room as free from dust as possible. There may occasionally be sensitivity to other environmental allergens, such as silk and wool, but the environmental allergens as a group are by no means so important in infancy as they are in later life.

#### RESULTS OF TREATMENT

Results of treatment are best in uncomplicated seborrheic dermatitis and in contact dermatitis when the cause has been found and removed. With some cases of atopic dermatitis in which there is marked sensitivity to cow's milk, brilliant results are obtained by the withdrawal of milk from the diet or occasionally by the use of goat's milk. The same sometimes hold true for other foods. In others, results are only fair, in many they are definitely poor, especially when there is erythroderma and profuse scaling, for which the name "atopic erythroderma" has been suggested. In this condition, in spite of definite sensitivity to various allergens, removal of these may have no effect nor is local treatment of any real curative value.

I have seen nothing in the literature, including my own contributions, which leads me to believe that any one really understands infantile eczema or that there is now any method of treatment, dietetic or otherwise, that is consistently and entirely satisfactory. And yet there is cause for encouragement in that appreciable progress has been made, particularly in atopic dermatitis, which has its roots deep in some of the most complicated and least understood phenomena of immunobiology.

While skilled local treatment is often very helpful, one cannot speak of "curing" an atopic person unless

there is at hand some method of making him nonatopic. There is no way of doing this at present, and the removal of allergens, while often effective and the best method of treatment based on etiology now available, does not really strike at the root of the trouble; in a way it is a surrender to an abnormal situation rather than a direct attack on it. Until there is a better understanding of the essential nature of atopy, this direct attack cannot be made.

The contact and mycotic elements, which I have not even discussed, still further complicate the situation in infantile eczema, and, in addition to these, infants have eczema-like eruptions of entirely obscure etiology which cannot be classified. One calls them "dermatitis" and lets it go at that. The picture is, however, gradually assuming a more definite shape. What is necessary now is an assembly of methodically and accurately collected facts, particularly as regards classification and the results of immunologic treatment. There is no disease in which it is more difficult to evaluate treatment, and it is necessary to be very conservative in attributing improvement to any therapy. Hypothesis and theory are necessary in the study of infantile eczema, as they are in the investigation of all natural phenomena. The trouble is that often in the literature of infantile eczema there have been too few solid facts to justify some of the conclusions that have been drawn.

Infantile eczema is not the exclusive domain of the allergist, dermatologist or pediatrician; it belongs to all of them, and each has something to contribute. Each must, however, explore the fields of the others more than has been done in the past if the best results are to be attained.

319 Longwood Avenue.

### Council on Industrial Health

THE COUNCIL ON INDUSTRIAL HEALTH HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. C. M. PETERSON, M.D., Secretary.

#### NOMENCLATURE IN INDUSTRIAL HEALTH

The Council on Industrial Health has from its inception considered that one of the first problems to which it might profitably give attention is nomenclature in industrial health. A committee of the Council was appointed to study the problem from a broad point of view and to prepare the following preliminary statement:

The language of industrial health is at present incapable of full expression within the strict confines of scientific terminology. It has been greatly affected by the particular environment of the worker and his special social relationships. For the most part the usages and idioms of industrial health have derived from the authority of court decisions, legislation and administration practices, the pronouncements of industrial organizations and of medical and nonmedical technical committees, as well as from the publications in the field. Variation in source and derivation has resulted in wide confusion. The general medical profession, therefore, needs to have available an analysis of the common terms used in industrial medical practice and to arrive at a clear understanding and a common acceptance of their meaning.

Any investigation which has for its purpose the inauguration of an industrial hygiene program must obtain accurate morbidity and mortality statistics. Frequently such statistical information is unavailable or is reduced in value through lack of adherence to uniform terms. Dictionaries and encyclopedias have supplied some assistance in understanding industrial medical terminology but, on the whole, there is little to which the medical profession

can turn at the present time for standard definitions of terms used in industrial health. The Council on Industrial Health, therefore, proposes to publish a compendium in which the frequently used terms of industrial medical practice will be defined and explained. It will be necessary to include explanations of certain expressions in fields of activity closely associated with industrial medicine. It is proposed that each term listed be provided with a brief and authoritative explanation. The ambiguities and perplexities of contemporary language in the field of industrial health will, as far as possible, be avoided. The compendium will not be a dictionary of terms in the ordinary sense or provide encyclopedic information, nor will its activity in any way duplicate or conflict with the work of the American Medical Association's Standard Classified Nomenclature of Disease.

It is hoped this compendium will serve a useful purpose to the general medical profession, acceptable to it as a first step toward the introduction of some measure of uniformity in the confusing terminology of today.

## Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

HOWARD A. CARTER, Secretary.

### BARACH-THURSTON JUNIOR OXYGEN TENT ACCEPTABLE

Manufacturer: Oxygen Equipment Manufacturing Company, 247 East Fifty-Sixth Street, New York.

The Barach-Thurston Junior Oxygen Tent is a portable unit designed for oxygen therapy. Complete equipment includes the tent canopy and elevating device, air-conditioning cabinet, motor blower, Oxy-Ator, Linde R50 Reducing Valve with gages, and an oxygen analysis outfit. It may be purchased without the two last mentioned items. The weight of the complete unit is approximately 85 pounds. It is mounted on five ball-bearing casters and is finished in hard synthetic enamel. All metal parts are chrome plated.



Barach-Thurston Junior Oxygen Tent.

The tent canopy is raised over the bed by means of a gear and rack appliance. It is adjustable from 48 to 68 inches from the floor. The canopy covers approximately three fourths of the bed. It has windows of cellulose acetate placed within spring steel window frames to protect against breakage. There are separate openings with slide fasteners placed at the side of the tent to provide for convenient nursing attention.

One claim made for the unit is that it will provide a concentration of approximately 50 per cent oxygen and maintain it for a flow of between 8 and 10 liters per minute. Any standard regulator or the Linde R50 unit may be used. An Oxy-Ator is attached to the reducing valve. Soda-lime is not used. The Oxy-Ator acts as a mixing chamber for removing carbon dioxide and conserving oxygen, according to the firm.

An air conditioning cabinet permits maintenance of the tent temperature between 50 and 70 F., with a relative humidity of from 35 to 50 per cent. The ice chamber, which is lined with tinned copper, has an ice capacity of 55 pounds. A brass air duct is so arranged that the air and oxygen entering the ice chamber must circulate through the ice before entering the tent, thus cooling the gas mixture.

The motor blower unit is housed in the lower part of the cabinet and circulates air through the tent in the desired direction by means of an adjustable deflector. According to the firm the air is changed with sufficient frequency to assure no

greater rise than 1 per cent in the concentration of carbon dioxide in the tent air without the use of soda lime. Two air ducts, one an inlet and one an outlet, are permanently fixed to the cabinet and may be extended in height.

In order to substantiate the claims made for the unit, it was investigated clinically by a competent physician and reported to give satisfactory service.

In view of the foregoing report, the Council on Physical Therapy voted to accept the Barach-Thurston Junior Oxygen Tent for inclusion in its list of accepted devices.

## Council on Pharmacy and Chemistry

### REPORT OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

PAUL NICHOLAS LEECH, Secretary.

### TRI-COSTIVIN NOT ACCEPTABLE FOR N. N. R.

A physician submitted a query to the Council office with regard to the advertising used by Professional Laboratories, Inc., for its product Tri-Costivin. The drug, which is claimed to contain the hormone cholecystokinin, is said to be suitable for oral administration. Cited in the bibliography supporting this statement is the article by Dr. A. C. Ivy on *Gastrointestinal Principles* which appeared in *THE JOURNAL* Aug. 17, 1935, and in the A. M. A. publication *Glandular Physiology and Therapy*. Inquiry was made of Dr. Ivy concerning the firm's use of this reference. His attention had previously been called by others to the advertising for Tri-Costivin and he had written to the firm under date of Oct. 15, 1937, in part, as follows:

"I note that you claim that Tri-Costivin contains the hormone cholecystokinin and that Tri-Costivin is taken orally. I desire to inform you that no evidence exists showing that cholecystokinin is active when given orally, and all evidence known to me is to the contrary. I, therefore, request that you withdraw from your future advertising any reference to my work on the subject of cholecystokinin. The reference to cholecystokinin is entirely misleading, and I consider it to be gross misrepresentation of the known facts."

In reply to Dr. Ivy a representative of the firm, Clifford A. Williams, vice president, pleaded that the actual statements as they appear in the advertising must of necessity be so condensed that there is little opportunity for qualifying statements. Continuing, the firm stated:

"However, in the basic literature on the product the following paragraph appears:

"The chief stimulus of gallbladder contraction thus far discovered is the hormone cholecystokinin (Ivy, p. 442). This hormone can be extracted from the mucosa of the upper part of the intestine of animals (Ivy). Although this hormone is considered effective only when administered intravenously (Ivy), some stimulating effect on the gallbladder seems to result from oral administration as well."

"The final clause of this paragraph is based upon our own clinical and laboratory tests, which obviously combined the use of the extract of duodenum gland with the other ingredients of Tri-Costivin in simultaneous action and indicate that so administered orally, does exert some stimulating effect on the gallbladder.

"We will, as you request, withdraw from our future advertising any reference to your work on the subject of cholecystokinin.

"We will go further, in order to clarify any confusion which might exist. We will insert in the small supply of the small folder to which you refer a slip sheet containing about the same text as is quoted above from the later literature. This same slip sheet will be inserted on the page in the already printed later literature containing a reference to your work in the bibliography.

"Then we will write each of the physicians who have shown any interest in the product, by requests for samples or additional literature, calling their attention to the fact that your work did not reveal any evidence of cholecystokinin activity when administered orally.

"Trusting that this will meet with your entire satisfaction, beg to remain,"

Through the kindness of Dr. Ivy, the preceding correspondence was made available to the Council.

In the firm's advertising it is claimed that:

"At last a rational therapy has been devised for that most frequent manifestation of gastrointestinal dysfunction—chronic constipation. The recognition that this disorder is due to a multiplicity of factors has led to the development of a product which directs treatment to the underlying causes rather than to superficial symptoms. In Tri-Costivin the physician has for the first time a product which contains all the substances most essential for the stimulation of normal gastrointestinal function [eureka!]."

The folder then goes on to describe the various constituents of this preparation. Vitamin B<sub>1</sub> and B<sub>2</sub> concentrates are attributed with "appetite stimulating powers" and "their ability to stimulate the gastric secretion of hydrochloric acid . . . for the maintenance of normal muscular tonus." "Another important ingredient" is said to be "lacto-banana concentrate" which is attributed with "aiding the elimination of putrefactive organisms." The product also contains "Trilactic (trade mark) combined with calcium lactate." Trilactic is described as a "polymolecular form of lactic acid" and is attributed with reaching "the lower portions of the intestine where it serves in changing the bacterial flora."

Under the heading "Important Hormones Included" the firm notes the presence of cholecysmon for promoting "fat digestion and assimilation," as well as "pure bile extract" and "cholecystokinin." The efficacy of Tri-Costivin according to the manufacturer is "due to the fact that it supplies, in scientific balance [sic] the eight essential factors indicated for the treatment of gastrointestinal dysfunction as evidenced by impaired digestion or assimilation, by autointoxication or chronic constipation." The firm states "It is a brilliantly rational product aimed simultaneously at many of the causes, rather than the symptoms of chronic constipation." Although the Council is not impressed by the various claims of this firm, the copywriter's selection of the verb "aimed" is admired. Its use in referring to a product containing eight different active ingredients recalls to mind the "shotgun prescription" typical of therapeutics a half century ago. Professional Laboratories, Inc., like those in the past who have prescribed such mixtures, fail to take into consideration that in any given case constipation may be due to any one or more of the factors which they discuss, as well as a great many others which they omit, and that it is desirable to determine which one of these factors is present in each given case before prescribing a remedy. It is possible then and only then to prescribe suitable therapy for that case.

If it could be granted that this is "a brilliantly rational product" it would have to be on the basis that the preparation is suitable for self medication. Obviously, in such case, it would not be necessary to know or determine the causes of chronic constipation in any given case, but simply to prescribe this remedy and hope that one of the "shot" will hit the mark. As already noted, the firm claims that its own evidence indicated that cholecystokinin is orally effective. Does its own evidence refer to the oral use of cholecystokinin or to the oral use of Tri-Costivin, which contains in addition cholecysmon and bile extracts? Just exactly what "Trilactic" and "lacto-banana concentrate" are is not clear.

It cannot be denied that such a mixture as this may prove useful in a certain number of cases of chronic constipation. It may also relieve symptoms in certain cases which sooner or later, and probably sooner, will require much more careful study than is needed to prescribe this scattered array of substances. Although the manufacturer may plead that the product is advertised only to the medical profession, the fact remains that the prescription of such a remedy as this requires little medical knowledge. The Council on Pharmacy and Chemistry has long ago decried all "shotgun prescriptions." In the opinion of the Council a pharmaceutical containing "eight active essentials" and claimed to be a "brilliantly rational product" is not worthy of further consideration on the basis of available scientific evidence.

The Council declared Tri-Costivin unacceptable for inclusion in New and Nonofficial Remedies because (a) it contains a multiplicity of active ingredients the combination of which is not warranted in scientific medicine, (b) it is promoted with unwarranted therapeutic claims based in part or indirectly on scientific evidence which has been modified to suit the case at hand, and (c) it is marketed under a name which naturally cannot give any indication of its eight ingredients.

## Council on Foods

### ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION AND WILL BE LISTED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED.

FRANKLIN C. BING, Secretary.

### BENEDETTO OLIVE OIL

*Manufacturer.*—Supreme Olive Oil Corporation, San Fernando, Calif.

*Description.*—Pure olive oil obtained from California olives.

*Manufacture.*—Ripe olives are crushed and oil extracted from the skin, pulp and pits by cold pressing. Water, soluble sugars and solids are separated and the oil is neutralized with caustic soda, washed with warm water, bleached with activated carbon and activated earth and filtered. The filtered product is then deodorized by fractional distillation to eliminate foreign odors and flavors.

*Analysis* (submitted by manufacturer).—Moisture 0.05%, total solids 99.95%, ash none, fat (ether extract) 100.0%, crude fiber none, carbohydrates none, specific gravity 0.913, free fatty acids (as oleic) 0.14%, unsaponifiable matter 0.52%, saponification value (Koettstorfer) 194, iodine value (Wys) 85.2, smoke point 123.9 C., melting point (fatty acids) 26.2 C., cottonseed oil (Halphen test) negative, sesame oil (Baudouin test) negative, peanut oil (Renard test) negative. Tea seed oil negative. Refractive index at 40 C. 1.4621.

*Calories.*—9 per gram; 255.6 per ounce.

### MRS. PALEY'S BABY FOOD— STRAINED CARROTS

*Manufacturer.*—Paley-Sachs Food Company, Houston, Texas.

*Description.*—Canned, cooked sieved carrots slightly seasoned with salt.

*Manufacture.*—Fresh carrots are washed, scrubbed, cut into small pieces, pressure cooked with the skins on, sieved, filled into glass jars, vacuum sealed and heat processed.

*Analysis* (submitted by manufacturer).—Moisture 90.0%, total solids 10.0%, ash 0.8%, fat (ether extract) 0.2%, protein (N  $\times$  6.25) 1.0%, reducing sugars as dextrose 2.3%, sucrose 1.4%, crude fiber 0.8%, carbohydrates other than crude fiber (by difference) 7.2%, calcium (Ca) 0.055%, phosphorus (P) 0.033%, iron (Fe) 0.0009%.

*Calories.*—0.3 per gram; 9 per ounce.

### (1) EMPSON'S BRAND TOMATO JUICE (2) KUNER'S BRAND TOMATO JUICE

*Distributors.*—Subsidiaries of the manufacturer: (1) The Empson Packing Company, Brighton, Colo.; (2) The Kuner Pickle Company, Brighton, Colo.

*Manufacturer.*—Kuner-Empson Company, Brighton, Colo.

*Description.*—Canned tomato juice, slightly seasoned with salt.

*Manufacture.*—Vine-ripened tomatoes are washed, hand selected, cored and again washed. The tomatoes are heated and the juice is extracted and homogenized. A closed system is used. Salt (0.58 per cent) is added and cans are filled, sealed and heat processed.

*Analysis* (submitted by manufacturer).—Moisture 93.1, total solids 7.0%, ash 1.2%, sodium chloride 0.8%, fat (ether extract) 0.1%, protein (N  $\times$  6.25) 0.8%, crude fiber 0.2%, carbohydrates other than crude fiber (by difference) 4.2%, titratable acidity as citric acid 0.5%, ascorbic acid, determined by titration with 2-6 dichlorophenolindophenol, 0.16 mg. per gram.

*Calories.*—0.21 per gram; 6 per fluidounce.

*Vitamins.*—As determined by chemical titration by the dye method the tomato juice contains approximately 16 mg. of vitamin C or 320 international units per hundred grams; 95 per fluidounce.



# THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, DECEMBER 3, 1938

## STRUCTURE OF PROTEINS

A fundamental problem of modern biologic science is the elucidation of the structure of proteins. An increasing number of biologically important substances have been demonstrated to be proteins.<sup>1</sup> Several enzymes have been isolated in crystalline form, and each of these has been found to be a protein. Several of the hormones are also now known to be proteins or protein derivatives. More recently has come the astounding demonstration that crystalline proteins of high molecular weight can be isolated from infected plant tissues and that these proteins have a physiologic activity identical with that attributed to an infectious virus.

The proteins resemble one another in that all proteins on hydrolysis yield the same amino acids, although proteins may vary widely with respect to the number of these fundamental units and the quantity of each which may be present in their molecules. Nevertheless the close resemblance among the products of complete hydrolysis of proteins makes even more difficult the explanation of specific physiologic activity on the basis of chemical composition. If the amino acid composition alone is responsible for the physiologic activity of proteins, why does one protein exhibit enzymatic activity, another serve as a hormone, and yet a third be apparently without any significant physiologic function?

As the chemical properties of the individual amino acids do not adequately account for the individuality of proteins, investigators have sought a solution of the problem in the mode of linkage of the amino acids to one another.<sup>2</sup> In addition, the fascinating problem of the configuration of the amino acids in space has been given consideration. This phase of protein structure has developed from a realization that the large molecular size of proteins must of necessity place some physical limitation on the theoretical possibility of the amino

acids existing joined to one another to constitute a long chain. Thus a folding or bending back of the protein chain on itself has been visualized, with the construction of cyclic structures to form definite patterns. If the definite sequence of these amino acids in the protein molecule can be established, and if the pattern of the arrangement of these amino acids in space can be constructed, the solution of the problem of protein structure approaches realization.

Through the efforts of Bergmann and his collaborators<sup>3</sup> at the Rockefeller Institute for Medical Research, the frequency of occurrence of the various amino acids in a number of proteins has been established. These investigations demonstrate, for the proteins studied, a definite periodicity existing for each amino acid in the peptide chain. That is, a given amino acid recurs at a regular interval in the molecule. In gelatin, for example, aminoacetic acid represents one third of all the amino acids, while proline represents one sixth and hydroxyproline one ninth. The frequency of occurrence of amino acids has also been determined for egg albumin, hemoglobin, fibrin, silk fibroin and other proteins. It is apparent that the existence of a simple arithmetical ratio among the numbers of molecules of amino acids is not fortuitous but must represent a regularity in the structure of the protein itself.

The establishment of the order in which the amino acids in a given protein may occur in the molecule leaves still unanswered the large problem of the manner in which these amino acid residues are arranged in space. That a definite pattern must exist seems evident from a variety of chemical and physiologic evidence. Experimental studies of the orientation of protein monolayers<sup>4</sup> is suggestive evidence for a definite pattern of protein structure. The x-ray studies of Astbury and his colleagues<sup>5</sup> also show clearly the existence of a framework or gridwork, particularly in the fibrous proteins like the keratins; more recently this has been demonstrated also for other proteins. Furthermore, biologic evidence of the type of enzyme specificity, immunity and the synthesis of specific tissue proteins suggests a definite pattern for protein structure.

A development of the concept that there must be a regularly repeated design for the manner in which the amino acids arrange themselves in space is the cyclol theory of protein structure proposed by Wrinch.<sup>6</sup> She suggested that proteins are made up of closed polypeptide chains consisting of amino acid residues. It is postulated that the hexagonal folding of polypeptide chains into cyclol units permits the construction of

3. Bergmann, M.: Harvey Lectures **31**: 37, 1935-1936; Bergmann, M., and Newmann, C.: *Ann. rev. biochem.* **7**: 99, 1938.  
4. Schmidt, C. L. A.: *Chemistry of the Amino Acids and Proteins*, Springfield, Ill., 1938, pp. 408-445.  
5. Schmidt: *Chemistry of the Amino Acids and Proteins*, pp. 315-325.  
6. Wrinch, Dorothy M.: *The Pattern of Proteins*, *Nature* **137**: 411 (March 7) 1936; *Structure of Proteins*, *ibid.* **138**: 651 (Oct. 10) 1936. Wrinch, Dorothy M., and Lloyd, D. J.: *The Hydrogen Bond and the Structure of Proteins*, *ibid.* **138**: 758 (Oct. 31) 1936.

1. *Proteins of First Importance*, editorial, J. A. M. A. **110**: 743 (March 5) 1938.

2. Vickery, H. B., and Osborne, T. B.: *Physiol. Rev.* **8**: 393 (Oct.) 1928.

molecules which might conceivably contain hundreds of amino acid residues in orderly arrangement and provides a characteristic pattern for the complex protein molecule. Although the cyclol theory appears to find strong substantiation from theoretical considerations and appears to offer an explanation of many facts in protein chemistry and physiology, there has been available little experimental work testing the validity of this theory of protein structure. Recently, however, Wrinch and Langmuir<sup>7</sup> have presented fundamental data supporting the cyclol theory of protein structure. Of added importance is the fact that this contribution is based on a study of the important protein hormone insulin. Utilizing available data on the x-ray crystal analysis of the insulin molecule, it has been demonstrated by means of mathematical analysis that these data support the polyhedral structure predicted for the insulin molecule on the basis of the cyclol theory. The fact that several suggested important features of the insulin molecule are confirmed also by the treatment given the x-ray data strengthens the validity of the cyclol hypothesis of protein structure and presents more clearly what appears at present to be the most logical of the many suggestions of protein patterns that have been put forward.

### ELIOT'S QUIZ

Many of the former pupils of Dr. Ellsworth Eliot Jr. will place their beloved mentor among the great and inspiring teachers of medicine. In a book called "Eliot's Quiz, 1889-1913," to which Dr. Eliot himself contributed an essay on extramural medical education, they have reflected medical teaching as it was in New York City fifty years ago. Attendance at medical clinics and lectures then was voluntary. Students could graduate at the end of three years without attending a single college exercise other than the final examination. Conferences and recitations were unknown. The student was a mere spectator at the clinics and only occasionally had opportunity at bedside clinics to listen to the physical signs of pulmonary and cardiac lesions. However, the competitive examinations for the highly prized hospital internships in New York hospitals were difficult. Recognizing the shortcomings of instruction methods in the medical colleges, some professors organized "quizzes," conducted often at night, for a limited number of students who paid a fee. Dr. Eliot conducted quizzes for twenty-four years, beginning in 1889. To his personality and methods of instruction many of his 476 pupils give the credit for arousing and inspiring them to success later in their chosen fields.

Six of his students came to be deans of medical schools, sixty-one to be full professors, twenty to be associate professors, thirty-one to be clinical professors

and 111 to be instructors in medical schools. From this group also came 104 visiting surgeons, 100 visiting physicians, 161 consultants and forty-four visiting specialists. Ten of this group became medical missionaries and ten became commissioned officers in the United States Public Health Service. During the World War, 178 of Dr. Eliot's quiz pupils served as officers of the army and nine as officers of the navy. Five of them have served in the medical corps of the United States regular army for many years. All members of Dr. Eliot's quiz, with eight exceptions, were graduates of the College of Physicians and Surgeons, New York. Although a college degree was not then generally required for admission to medical schools, 402 of the 476 men in the quiz had graduated from college before going to medical school.

In editing this tribute to his teacher, Dr. Howard Fox has included short biographic sketches of practically all the members of the quiz as probably the best way to show Dr. Eliot the results of his methods of teaching.

Dr. Eliot was large and towering physically and his personality awe inspiring. His great force of mind and body aroused his students to work. A former student writes: "He centered on me all the horrors of his sarcasm, his kindly wit, his stinging rebuke, his concise statement of fact, and his power to put the fear of God in any one who failed to properly prepare himself for those quizzes through which we went." On one occasion Dr. Eliot told a student that at the next session he would be required to name each and every articulating facet of the tarsal bones and their articulations. The student now writes with pride that he did not submit then nor has he at any time since submitted to any such memorizing test as this. Another writes of a "beautiful spring morning in May when I was seated in Dr. Eliot's quiz gazing out of the window. Suddenly I heard his great booming voice say 'Jackson, what are you doing?' I replied that 'I was wishing the hell that I was out of here enjoying God's beautiful sunshine out of doors.'"

At times, the quiz was conducted from 10 p. m. to midnight. Later classes rebelled at these hours and they were changed from 9 to 11 p. m. The quiz was held in the back room of the ground floor of the English basement house in which Dr. Eliot lived. Along three sides of this room were chairs and in the center was a desk piled high with medical journals. Williams writes: "Here sat the old man leaning back in his swivel chair with his feet on the desk. As a part of the evening's ritual he always smoked a cigar and sipped a glass of milk."

When the medical schools finally began to teach medicine, the extramural quizzes became unnecessary and one after another they disappeared. However, "The Quiz Medical Society" was formed in 1897 at a

7. Wrinch, Dorothy M., and Langmuir, I.: *J. Am. Chem. Soc.* **60**: 2247 (Sept.) 1938.

meeting in New York City. From time to time this society has given "The Old Man" loving cups, once thirty years ago when he was engaged to be married, later when he became a father and more recently when Dr. Eliot's days had numbered three score and ten. The tradition of medicine is replete with similar instances, reflecting a personal relationship between instructor and student almost peculiar to medical education. Such admirations are a part of the humanity which is an integral part of the medical soul. Will the highly standardized impersonal teaching associated with present trends in medical teaching be able to develop any substitute to compensate for the loss of these relationships? The question is fundamental to the whole future of medical care.

## Current Comment

### SULFANILAMIDE-PYRIDINE

The use of sulfanilamide in the treatment of pneumonia has not been sufficiently encouraging to warrant recommendation of this product to replace specific antiserum. While sulfanilamide has value, the results are not striking. The fact, however, that this chemotherapeutic agent does possess some value in infections due to pneumonia led to the investigations of derivatives of sulfanilamide with a view of obtaining one which might have a more definite chemotherapeutic effect. Early this year English workers announced that the pyridine derivative of sulfanilamide described as 2-(p-aminobenzenesulfonamide)-pyridine ( $\text{NH}_2\text{-C}_6\text{H}_4\text{SO}_2\text{-NHC}_5\text{H}_4\text{N}$ ), or sulfanilamide-pyridine, had been found to protect mice against pneumonia invasion to a much greater extent than was possible with sulfanilamide. The drug is patented and marketed in Great Britain by May & Baker under the nondescriptive name of M & B 693,<sup>1</sup> or "Dagenan." Merck & Co. Inc., the American firm which has obtained the patent rights for the product in this country, has, to its credit, not placed the product on the market; instead it has placed it in the hands of competent investigators in chemotherapy and pneumonia to determine more definitely its dosages, advantages and limitations. While published reports containing the details of the studies thus far are not available, THE JOURNAL has received communications from a few investigators, all of whom agree that the product has promise in the treatment of certain types of pneumonia. Fortunately the preliminary studies are being made before the product is widely distributed. With any new preparation, careful animal experimentation must be followed by cautious clinical trials to determine its pharmacologic effects. The substance has not yet been submitted to the Council on Pharmacy and Chemistry but the firm undoubtedly will submit

the product before it is actively promoted. The Council is also considering the choice of a name for the substance which may be used in scientific literature. Recently the press devoted much space to the development of this product. The demand for it might have yielded serious consequences except that the new food and drug law prevents its sale over the counter. Moreover, Merck & Co. is cooperating fully in determining both the usefulness and the hazards associated with the product before making it generally available.

### FIRST ANNUAL CONGRESS ON INDUSTRIAL HEALTH

One of the first activities of the Council on Industrial Health of the American Medical Association is the conference to which leading representatives of the groups interested in improving the physical and environmental status of the working people are being invited. The program appears on page 2128 of this issue of THE JOURNAL. The papers in this inaugural conference will review past accomplishments and appraise future needs. The discussions will be confined largely to the medical organization approach to industrial health problems in contrast to the purely clinical discussions which occur at many other meetings. In addition, sections of the program will, for purposes of orientation, outline the contributions and programs of governmental and independent organizations. Aside from its primary value of acquainting the profession with activities now going forward, it is thought that there will be the added advantage of reducing duplication of effort by agencies in industrial health. The sponsorship of a forum of this character by the American Medical Association amply indicates that the physician has a fundamental interest in seeing that medicine is properly represented in discussions involving health control of the employed population. Even more important, it is hoped that this meeting and the following meetings will represent in the eyes of the profession its own determination to find out what its best and most effective contribution should be toward improving the health of the individual worker.

### COMMERCIAL MISUSE OF INVESTIGATORS' NAMES

The report on Tri-Costivin in this issue of THE JOURNAL (p. 2118) calls attention to an embarrassment frequently suffered by reputable scientists through the misuse of their names in the commercial exploitation of pharmaceutical preparations. As in the instance reported, authors can usually obtain promise to delete their names and reference to their articles from such advertising copy once they object to the firm responsible for the infringement. The misapplication of purely scientific material in the promotion of new pharmaceutical preparations is unfortunate. This is especially apparent at a time when many leading manufacturers are spending huge sums to provide adequate facilities for research.

1. American physicians long ago gave up such unscientific methods of naming products as by letters or numbers. "Dagenan" is a name which in no way indicates the composition of the product, and its use is to be deprecated.

# ORGANIZATION SECTION

## FOR A FREE PROFESSION

Speaking as a member of the Committee on Economics of the Medical Society of the District of Columbia, Dr. Thomas E. Mattingly recently gave to the press a statement of his views of objectives of medical organization. The statement is so succinct and so well phrased that it would seem to deserve wide circulation. Dr. Mattingly, who incidentally appeared before the Grand Jury which is investigating organized medicine, said:

I am a member of the Medical Society of the District, and I believe in all the objectives of organized medicine.

We would like the people of Washington to be patient with us—to have faith in us and to believe that our social objectives are just as altruistic but infinitely less speculative than those who seek our indictment.

We believe that here on the weakest sector of human rights, a voteless community, we are using the only means we have to prevent our own destruction and degradation. Surely no one can expect us to initiate or be party to our own undoing.

Perhaps there has been an element of error in our method but men in desperation, fighting against odds—for what they regard as their very existence—are just as prone to forget the niceties of warfare as those who wage it.

Our objects are simple, and we believe self justified. No matter what method of medical practice is finally evolved, common sense tells us that it should embody all the safeguards and guaranties which made us cherish the old.

First and foremost is the unqualified right of the patients to choose their own doctor and determine the conditions under which he may continue to serve them.

The second, that no subsidy of taxpayers' money be given one group of citizens which is not available to every other citizen in the same circumstances.

Third, that the doctor be obliged to compete for his patient's favor and patronage and that his security be earned by merit and not apportioned by political favor.

Four, and this is in the nature of a conclusion, that under no plea of emergency should the patient be persuaded to delegate the control of medical practice to those who promise more than reason and experience tell us they can deliver. Whatever the faults of the present system of medical care, it has not

added to the heavy burden the taxpayer must bear in generations to come. It at least has the virtue of paying its way.

These are principles in equity and even if the old system must perish, these corner stones of our progress must, and should, remain.

Finally, we would like to call attention to the grave dangers, the terrifying potentialities, of allowing any agency of government other than the lawmaker to legislate through subterfuge, even if the end desired should seem to justify such a means. We hold that, if laws are old and antiquated and are not applicable to a modern need, it is the province of the legislator to change them.

It is not amiss to remind those thoughtless enthusiasts who have no scruple against unconstitutional and undemocratic short cuts to their political rendezvous with power that it was by this very mechanism that monopolies, in the sense of the anti-trust laws, came into being. By interpreting the "due process clause" of the fourteenth amendment to mean that it applied to corporate property as well as to the newly liberated slave, the corporate fiction was endowed with human rights. Instead of the lawmaker making a law to apply specifically to new social and economic conditions, it allowed the legalistic mind to interpret a law dealing with a human being who had ceased to be property as being applicable to property that had become a human being.

We hope that it is neither amiss nor presumptuous to ask every true liberal who believes in social progress, attained by equity and evolution rather than by fiat, to join us in our desperate stand to prevent a repetition of the grave errors of the past. Forgive us if we have offended. We will try with every resource at our command to earn your further favor.

## AMERICAN MEDICAL ASSOCIATION STUDY OF MEDICAL CARE

### Seven Nebraska Counties

Seven counties in Nebraska have returned their summary sheets in the Study of Need and Supply of Medical Care. These seven counties are Pawnee and Nemaha in the southwestern corner of the state, Nance, Howard and Franklin in the central and southern parts, and Sioux and Dawes in the northwestern corner of the state. These counties have an area of 4,861 square miles and a total population of 65,772 (U. S. Census 1930). Practically all the people are engaged in farming. There are only two counties which have incorporated cities with more than 2,500 inhabitants (Dawes with the city of Chadron, 4,606, and Nemaha with the city of Auburn, 3,068, U. S. Census 1930).

In the whole area there were only 237 people engaged in manufacturing in 1929. A negligible number were engaged in mining and forestry. Consequently, the income of the majority of the inhabitants in the seven counties is obtained from farming.

Nebraska, especially the western part, is in the area known as the Great Plains, where arid and semiarid years are so frequent that they create an exceptionally difficult agricultural hazard. In this area, conditions of distress due to climatic adversities are very evident and much of this land is submarginal for agriculture.

Two thirds of the years from 1910 to 1934 were arid or semiarid for the Northern Great Plains area.<sup>1</sup>

This report also includes a study on the income of the inhabitants of the Great Plains area in which it stated that 60 per cent of the income was derived from the production of wheat and other grains. The other 40 per cent is derived chiefly from stock ranches. The average annual net income from wheat production on a 640 acre farm in this area between 1912 and 1934 was \$1,007.97. This includes years of bumper crops and high prices. In twelve of those twenty-one years there was an actual net loss, including the years 1933 and 1934. In general, regardless of the use of the land in this area, periods of heavier than average rainfall and unpredictable droughts at irregular intervals are responsible for severe economic distress.

The report concludes that in most cases farmers in the semiarid area of the Great Plains cannot earn more than a meager living from the land. A livable income, it is believed, can be obtained only through government subsidy, which would be financially prohibitive for a long period of time.

1. Migration and Economic Opportunity. Report of the Study of Population Redistribution, Industrial Research Department, Wharton School of Finance and Commerce, University of Pennsylvania Press, 1936.

The following figures, taken from the Consumers Market Data Handbook, Department of Commerce 1936, will give some indication of the average net income and the number of persons on relief in Nebraska, and in the specified counties:

There was a total of 24,939 income tax returns for the state, 0.7 per cent of the total number of returns for the whole United States in 1933. There were 2,499 persons who reported incomes under \$1,000, 16,587 between \$1,000 and \$5,000, 4,023 between \$3,000 and \$5,000, 1,363 between \$5,000 and \$10,000, 436 between \$10,000 and \$40,000, and thirty-one reported an income of \$40,000 or over. It is evident that the majority of the people who filed income tax returns had a net income between \$1,000 and \$3,000, but only 1.8 per cent of the total population for the state made an income tax return, and only 0.7 per cent of the persons living in the seven counties had sufficient net income to necessitate filing income tax returns. These seven counties contain 4.7 per cent of the total population in the state.

From July 1934 to July 1935 the average number of persons on relief rolls in the state was 171,933, or 12.5 per cent of the total population, while the average number for these seven counties was 6,175, about 9.4

pharmacists made no report on the number of prescriptions compounded free, at cost or at reduced fees.

The county, with the aid of federal funds, provided medical care for the indigent. No private agencies provide care for the indigent. In determining a patient's ability to pay for medical services, the hospital and the welfare agency considers each case individually. During 1937 there were no cases of persons in need of medical care who were unable to obtain necessary services from either the hospital or the physician.

Seven of the eight physicians reported that they were performing preventive medical service, but it was estimated that only 10 per cent of the children who entered school for the first time in 1937 were successfully vaccinated against smallpox. A physician or a midwife was in attendance at all obstetric cases during 1937, and there were no known deaths from childbirth. The infant mortality rate was not given. The physicians are not receiving any kind of subsidy or guaranty to encourage them to remain in their community.

Persons and Organizations Which Provide or Arrange for Medical Services

County	Population	Physicians	Dentists	Pharmacists	Nurses	Medical Relief Agencies	Public Health Departments	Hospital Beds	No. of Miles the Nearest Physician Is from Any Person
Pawnee.....	9,423	9	5	13	1	1	1	126	10
Nemaha.....	12,356	12	8	13	1	1	1	123	6
Nance.....	8,718	6	5	5	3	1	1	13	20
Howard.....	10,020	7	5	7	3	1	1	5	15
Franklin.....	9,091	7	4	7	1	1	1	1	30
Sioux and Dawes....	16,160	11	8	8	2	2	2	35	30

per cent of the total inhabitants in these counties. The percentage of personal income tax returns and the percentage of persons on relief in these seven counties are low compared to the percentage of persons making income tax returns and the percentage of persons on relief in the state. However, since none of these counties have large cities in which there are more people making tax returns, and more persons on relief than in rural areas, these seven counties may be considered average rural counties in Nebraska.

Pawnee County

During 1937 the one hospital in Pawnee County reported 80 per cent occupancy in the private rooms and 75 per cent in the semiprivate rooms and wards. The daily hospital rates are \$3.50 for a private room, \$2 for a semiprivate room and \$1.50 in wards. The hospital does not have an outpatient department, and no clinics are in operation by the health department, relief agency or any other organization. Health supervision for the schools, under the control of the board of education, provides for examinations of the students.

The physicians of Pawnee County reported that during 1937 they had given free service to 3,000 persons, and the dentists that they had given free care to 300 persons. The hospital provided services to 143 free patients, 499 pay or part-pay patients and to twelve public charges, which made a total of 1,430 patient days of hospital care for free patients, 4,234 for pay or part-pay patients and 1,500 for public charges. The

Nemaha County

In Nemaha County during 1937, 650 persons were given free services by the physicians and 225 by the dentists. The hospital provided care for 250 pay or part-pay patients, forty public charges and eighteen free patients, which made a total of 1,560 patient-days for pay or part-pay patients, 290 days for public charges and 340 days for free patients. The rates for private rooms are \$3.50 a day, semiprivate \$3. The pharmacists provided forty-five free prescriptions and 150 prescriptions at cost or reduced fees. All the pharmacists reported an increase in the sale of medicine on physicians' prescriptions for the year 1937 as compared with 1936 in relation to the number of sales of home remedies or "patent" or proprietary remedies.

All indigent persons needing medical services may receive the services from the local hospital or physicians, who are then paid by the county relief commissioner. Indigents with serious illnesses are sent to the state university hospital, and the state also maintains institutions for the blind, deaf, crippled children, tuberculous patients and the feeble-minded, to which the county sends suitable cases. In determining the indigence of a person the county relief commissioner investigates a person's financial condition.

It was estimated that 400 persons requested medical care from the health department, and in every case they were provided with the necessary medical services. No persons were reported in need of medical care who did not receive such care by the relief agencies, physicians, dentists, nurses or hospitals.

All the physicians perform preventive medical services in private practice and for the health department. Of each thousand children born alive during 1937 it was estimated that 200 were immunized against diphtheria. All births were attended by a physician or a midwife, but only a small percentage of the children who entered school for the first time in 1937 were successfully vaccinated against smallpox.

Medical Care in Nance County

From Nance County it was indicated that during 1937 the hospital cared for 168 pay and part-pay patients, thirty-two public charges and seven free patients for a total of 1,042 patient-days of hospital care. The bed occupancy during 1937 was 96 per cent. The minimum daily rate is \$3 and the maximum is \$4. During this period physicians estimated that they gave

free services to 812 persons and the dentists to 145 persons. Pharmacists provided 150 prescriptions without charge and 150 at cost or reduced fees.

Persons in need of medical care, but unable to pay for it themselves, were provided for by the county. The county agents in charge of relief determine whether they are entitled to county aid for medical services, and they stated that accidents and sudden illnesses made up the greatest expense for the county with regard to medical care. There were no instances of medical care being refused to any person by the hospital, physicians or dentists. If a person was unable to pay for medical services, the hospitals and the doctors obtained their fees from the county or state relief agency. A physician or a midwife was in attendance at all obstetric cases.

#### Howard County

From the Howard County summary sheet the following information is obtained: Physicians gave free services to 616 persons, and the dentists to 142 persons. The hospital provided services to forty-five pay and part-pay patients, ten public charges and two free patients. The nurses made eighty-six visits during the year, 50 per cent of them without charge to the patient. The pharmacists compounded 242 prescriptions without charge and 147 at cost or reduced fees. Three pharmacists reported an increase in the sales of medicine on physicians' prescriptions for the year 1937 as compared with 1936 in relation to the number of sales of home remedies or "patent" or proprietary remedies. County relief agencies provided the necessary medicines to persons on the relief rolls.

During 1937 there were no instances of persons in need of medical care but unable to obtain it. County relief agencies, with the aid of state and federal funds, provided medical care to all persons in the county needing medical treatment who were financially unable to secure funds to pay for it themselves. In determining who was entitled to receive county aid for medical services, the county relief agency investigated the applicants' financial status.

#### COMMENTS ON CONDITIONS

Six of the seven physicians performed preventive medical services in private practice and four performed preventive services for the county relief agency. The board of education provides health supervision and examinations for school children. Comments which accompanied the summary sheet for this county are as follows:

A comment from a dentist seems to cover the whole situation here very well:

I believe that people as a whole are being cared for quite well even in these times of financial stress. Surely they are getting far better attention than they ever could under a system of socialized medicine, where there would be no end of red tape and professional quackery. A professional man in these days at least does what he thinks is right in order to uphold his reputation, which is a very valuable asset. Under any system of governmental salaries or cut fees the professional standards can only sink to a new low. Of course, people kick against the medical professions but they haven't seen socialized medicine yet or they would have something to kick about.

The following is a summary brought out by the others:

1. The less interference with the profession, the better the morale of both patients, public and doctors.
2. Low income groups as WPA need plans by which they can receive medical services and then pay for them. Inability to pay and not the doctor's refusal to care is reason why many do not seek attention sooner.

3. Local hospital facilities not adequate.

4. The need for free medical services has multiplied during the last few years. Can be supplied through proper arrangements with county boards. Preventive inoculations for indigent cared for through schools and P.-T. A. organizations.

5. People are receiving medical service now and the professions are giving time freely to all that are in need. Public funds should be applied to help both the patient and the doctor, dentist and nurse.

6. Medical services should be supplied to all but the morals in the recipient and his initiative are held on a higher plane where a financial interest is involved. No cases turned down regardless of finances.

#### Franklin County

Franklin County reports that 237 persons were provided free services by physicians and fifty-six by dentists. Pharmacists made up 286 free prescriptions and 151 prescriptions at cost or reduced fees. Indigent persons in need of hospitalization are sent to the university hospital in Omaha. Four persons were reported to have been unable to receive hospital care there because the hospital was overcrowded. Because of lack of funds 100 persons, mostly dental patients, were reported unable to obtain necessary care. This made a total of 104 persons in the county unable to obtain medical, dental or hospital care during 1937. All the physicians reported that they were active in performing preventive medical services in private practice and for welfare agencies.

With regard to medical care for the indigent, the report stated that up to three months ago the county guaranteed to pay the bills of the indigent for necessary medical care. Hospitalization cases were sent to the state hospital at Omaha. Now Franklin County has contracted with the Brewster Hospital, at Holdrege in Phelps County, to handle all the indigents in need of medical care. This arrangement does not provide the indigent with free choice of physician or hospital, and the county pays the same rates for hospital services as it was charged by any of the other nearby hospitals. The resettlement agency of the federal government will pay one half of the bill for medical services received by its clients provided the fees are reduced from 50 to 75 per cent. At the present time the county has spent all the funds apportioned for medical care for the whole year. A new state law prevents the county from contracting any debts, and consequently physicians must continue to provide the indigent with necessary medical care with no remuneration from the county. It is further stated that there are about 2,500 persons on relief in this county and that, unless the county makes a different arrangement whereby it will pay adequate fees for medical care rendered to the indigent and also provide these persons with free choice of physician and hospital, it will be impossible for the physicians to earn enough to cover their living expenses.

The following comments will indicate the necessity for the county to assume the responsibility of paying for medical care of the indigent.

#### 1. Physicians and Dentists:

(a) There is need for much restorative work on teeth. Indigent cases should be paid through a local county agency.

(b) Care of indigents is usually paid by the county from the poor aid fund, although such pay is slow in forthcoming and very often inadequate.

(c) Pay through county, resettlement and other governmental agencies is slow and usually at a greatly reduced fee.

(d) Poor crops prevent many people from getting or seeking medical care because of insufficient funds. These people are not acutely ill but are not well. The county and other agencies will take care only of persons who are seriously ill. Other



persons cannot be taken care of by county funds because the county itself is usually financially embarrassed. If the county could be provided with adequate funds, it would be able to take care of the pay for indigent cases.

(c) Resettlement and other governmental agencies expect physicians to do work at greatly reduced rates while the employees of these agencies are all getting better than average salaries. I believe the county should be allotted funds to be used entirely through the local county agency for cases recommended by the local physician.

## 2. Pharmacists:

(a) Should be worked out by medical and pharmaceutical agencies themselves.

(b) Should have more doctors in small towns, since going to another town or calling in a doctor from another town involves a much greater expenditure.

(c) The doctors and druggists should get at least some of their money in caring for the indigents from the government or state.

(d) Provide the county with adequate funds and the whole thing could be handled very nicely by our doctors and druggists. But we do not want any socialized medicine.

## In Northwestern Nebraska

The Northwest Nebraska County Medical Society, which includes the three counties of Sioux, Dawes and Sheridan, reported on only two counties, Sioux and Dawes. The board of education provides health inspection for school children, and eight physicians perform preventive medical services in private practice. It is estimated that 60 per cent of the children who entered school for the first time in 1937 were successfully vaccinated against smallpox. Free medical services were provided for 260 persons, and free dental care was given to seventy-one persons.

There is no standard arrangement or procedure used by the county to determine a person's inability to pay for medical services or to provide relief clients with the necessary medical care. The individual physician or dentist provides free medical care to all indigent families requesting such care whom he believes to be

deserving of free services. The known chronic indigents and malingerers are unable to secure any further medical care except in emergency cases. The county does not provide any clinic or hospital services for the indigent. Even under these adverse conditions, physicians and dentists believe that no deserving person has been denied the necessary medical or dental care during 1937; however, the Red Cross agency reported ten such cases.

No comments were attached to the summary sheet but the county medical society attached the following recommendations pertaining to the need and method of providing and paying for medical services to the large number of people on relief.

## Recommendations:

1. Direct appeal to the physicians in smaller communities, by representatives of organized medicine to organize for economic reasons as well as educational. Technical articles and talks do not appeal to many physicians in smaller towns. Stress economic value of united effort.

## 2. Publicize:

(a) Physicians' investment in education, overhead expense and hours of work.

(b) Rapid advance in medical knowledge through research—requiring study, "refresher" courses and postgraduate work.

(c) Necessity of public accepting responsibility for health of the indigent.

(d) The right of physicians and dentists to expect pay for services the same as laborers, merchants, relief and social workers and/or politicians.

(e) The right of each physician or dentist to accept or reject service to indigents on a reduced fee basis.

(f) The right of each patient to select his own physician.

(g) The value of preventive medicine and medical supervision of youth.

3. Supply necessary medical and dental care to the indigent through local agencies in cooperation with organized medicine and dentistry.

4. Keep service on a fee basis so that better and more complete service will be encouraged.

## TRIBUTES TO PHYSICIANS

### GORDON B. MAURER

Amidst the tumult and shouting relative to the physician and his work there continue to appear in various newspapers throughout the nation tributes to doctors who have served valiantly in their careers. Recently a young physician, Dr. Gordon B. Maurer, died in Margaretville, N. Y. The *Catskill Mountain News* contained this tribute to him and to his work:

### MOUNTAIN DEW

Thirteen years ago there came here a city chap, trained in one of the great universities.

The other members of his class went to "big towns."

He, with the best records of them all, wanted to begin the practice of medicine in a country village.

He had compiled a list of prospective communities. He looked over several and chose us.

An untried city college boy—with magic hands, a keen vision, and uncanny knowledge of both the human body and the soul which activates it.

Soon after arrival he was called upon to care for a life given up as lost. He saved it.

He began to save others. He worked day and night. When he did not have proper apparatus or appliances he built some. When the snows kept him from patients he constructed a snowmobile.

Neither storm nor night nor mud nor snow kept him from the sick.

He took people into his home. It became a veritable hospital. The fame of the boy spread throughout the section. Men and women from all walks of life asked for his attention.

The community built a hospital that he and others might the better care for those who needed care, medication and operation.

He continued. When a tired body all but gave up he took a year out and returned to Yale for special work that he might come home and serve better.

He had tired of city pastimes. The lure of the country had been breathed into his soul. Camp, rod and gun, open fires, life in the great outdoors gave zest, relief, happiness.

He loved our hills, our mode of life; he knew our ambitions, he smiled at our shortcomings.

He gave freely, much of the work he did was without charge. Few knew the extent of his help to those who needed help. He served as few had ever served here before.

He was physician, parson, priest, confessor—we told him both our physical and mental troubles and he put us back on the road to reason and living.

Thirteen years he served. It was a life work worth while. Today our hearts are numb at his loss, our senses befogged to know how to live without him. May we turn from the tragedy of the golden Indian summer morning that knew his death.

And in the bleak days of the approaching Thanksgiving season thank God for those thirteen years.

Yours truly,  
The Mountaineer.

ROY G. WERNER

In Akron, Ohio, there died not long ago Dr. Roy G. Werner. The following tribute, written by Anthony Weitzel, appeared in the Akron (Ohio) *Beacon Journal*, under the column headed "The Town Crier." (Several paragraphs that appeared in the original publication have been omitted.)

There is nothing I can write here that would add to the beauty or the stature of the glorious human monument that was the life of Dr. Roy G. Werner.

I can only echo the grief that lives today in the hearts of those hundreds of mothers and fathers of Akron who owe their most priceless gifts to his great skill.

I know that grief. Saturday night when I got home my wife was at the telephone, her eyes filled with tears. She said "Dr. Werner is dead!"

Bruce played at her feet, absorbed in the mechanics of a toy truck. We stared at the boy, my wife and I, and our thoughts went back to a chill February dawn, nearly four years ago.

There was no Bruce then. There was only a frantic newspaperman pacing the corridors of City Hospital and a sweet courageous girl somewhere upstairs bravely entering her hour of travail. . . .

After a long, long time, the zero hour came, very suddenly. The telephone girl called me from my pacing. She said "Your wife has just been taken into the delivery room." Then for an awful space there was no word.

The minute hand on the corridor clock seemed to hang motionless against its white face. The world stood still. Then the phone rang and the girl said "It's a boy . . ."

I couldn't believe it for a long moment. Then I raced upstairs. The girl slept, wan and white, on a wheeled cot. A precious little bundle in a nurse's arms made strange gasping noises.

Dr. Werner, still in his white hospital clothes; leaned against the delivery room door, his face drawn with exhaustion.

He said, softly, "Well, I guess we made it . . ."

I felt a twinge of pity for him then; he seemed so utterly spent. He seemed to have poured his very soul into the battle for the life of that little bundle in blankets.

I said to him "I guess you'll be glad to get home and go to bed!"

"Oh," said Dr. Werner, "I've got another delivery coming along in a little while."

That was the doctor's life, as it must be the life of all good physicians. Rich women and poor came to him, with their precious unborn, and to each he gave the same full measure of devotion.

Day after day, year after year, he threw his skill and his strength and his great heart into the fight against death. Nearly always he won, but each victory took its toll of him. Each time he brought a new life into the world he literally gave a part of himself as a hostage to death.

So, unselfishly and humbly, he built his monument, that must live as long as the memories of a generation of mothers. And because he gave so greatly of himself, death came early to claim its hostage, a great and kindly man.

## THE COOK COUNTY HOSPITAL

### A Statement by the Council on Medical Education and Hospitals

Widespread interest in the standing of the Cook County Hospital seems to warrant a review of the events of the last few years as far as they concern relationship between the hospital and the American Medical Association.

The Council on Medical Education and Hospitals in February 1935, after nearly a year of fruitless correspondence with the officers of the hospital and the Civil Service Commission, withdrew from the Cook County Hospital its approval as far as the training of interns is concerned.

In June 1937, in order to protect those interns who received appointments subsequent to February 1935, the Council granted approval to the Cook County internships for a period of one year from July 1, 1937. On July 1, 1938, such approval automatically lapsed.

In the meantime the County Board appointed a Survey Committee consisting of:

Dr. Irving S. Cutter, dean of Northwestern University Medical School and Superintendent of Passavant Hospital, chairman.  
Miss Veronica Miller, superintendent of Henrotin Hospital.  
Rev. John W. Barrett, diocesan director of Catholic hospitals.  
Dr. A. C. Bachmeyer, director, University of Chicago Clinics.  
Mr. Asa Bacon, superintendent of Presbyterian Hospital.  
Mr. Charles A. Wordell, director of St. Luke's Hospital.

The personnel of this committee inspired the highest confidence and gave to its conclusions unimpeachable authority. With these recommendations the Council found itself in fullest accord.

One of these recommendations concerned the appointment of a Citizens' Advisory Committee composed of well known public spirited men to which the County Board might look for advice in all matters pertaining to the organization and operation of the Cook County Hospital. Such a committee was duly appointed.

The Survey Committee called attention to the fact that the professional services in the hospital had not been brought up to present day standards, that the records of patients were inadequate and that there was need for a more systematic

review and analysis of clinical work. Interns were given large responsibilities without sufficient guidance from older and more experienced men, the nursing service was inadequate and the management of the outpatient department was unsatisfactory. In the maintenance of the physical plant many deficiencies were noted. In the judgment of the committee, steps should be taken immediately to (a) provide capable and adequate management, (b) relieve the acute shortage of nursing service in certain wards, (c) give effect to a comprehensive program of maintenance and improvement of equipment essential to the proper care of patients, (d) provide essential new equipment and supplies as required for the care and treatment of patients, (e) give careful consideration to allocating various services throughout the hospital to the approved and accepted medical schools and also a service to be staffed by physicians who have had the examination as required but who may not be members of the faculty of any of the approved and accepted medical schools, (f) promote economies and improvements in operation in all departments and (g) develop a comprehensive long range planning program to care adequately for the indigent hospital needs of Cook County.

Of all the recommendations of the Survey Committee, however, the most important was the requirement that a trained and experienced hospital administrator be appointed as the directing head of the County Hospital. After unsuccessful efforts to secure the services of a well qualified hospital director, the board appointed as warden a retired army officer, Brigadier General Manus McCloskey. The most serious obstacle in the way of getting an administrator with the requisite training and experience was the Illinois statute governing the appointment of "warden." Until such time as the state law can be amended so as to provide satisfactory tenure and eliminate a residence requirement for this position, it may be that the appointment of General McCloskey was the best that the County Board could do.

However, under these circumstances it must be recognized that it is absolutely essential that there be immediately provided a full time assistant to General McCloskey who is a physician and who has had successful experience in hospital management. Negotiations to this end are now under way.

## OFFICIAL NOTES

## COUNCIL ON INDUSTRIAL HEALTH

The first Annual Congress on Industrial Health, sponsored by the American Medical Association, will be held Monday and Tuesday, Jan. 9 and 10, 1939, at the Palmer House in Chicago.

The program of the two day session has been arranged as follows:

## OPENING SESSION, MONDAY MORNING, 9:45

*Report of the Council on Industrial Health*

Stanley J. Seeger, M.D., Chairman, Milwaukee.

## SYMPOSIUM ON INDUSTRIAL RELATIONSHIPS

*The Physician in Industry and Organized Medicine*

Irvin Abell, M.D., President, American Medical Association, Louisville, Ky.

*The Physician in Industry and the Employer*

C. D. Selby, M.D., President, American Association of Industrial Physicians and Surgeons, Detroit.

*The Physician in Industry and the Employee*

Loyal A. Shoudy, M.D., Chief of Medical Service, Bethlehem Steel Company, Bethlehem, Pa.

*Industrial Health and the Private Practitioner*

R. L. Sensenich, M.D., Trustee, American Medical Association, South Bend, Ind.

## MONDAY AFTERNOON, 2:15

*The Program of the American College of Surgeons in Industry*

Frederic A. Besley, M.D., Chairman, Committee on Industrial Medicine and Traumatic Surgery, American College of Surgeons, Waukegan, Ill.

*Uniformity in Workmen's Compensation Procedure*

Voyta Wrabetz, Chairman, Industrial Commission, State of Wisconsin, Madison.

*Bases for Cooperation Between Insurance and the Medical Profession*

Ambrose Kelly, American Mutual Alliance, Chicago.

*A Program for Committees on Industrial Health in the State Medical Societies*

A. D. Lazenby, M.D., Chairman, Committee on Industrial Health, Medical and Chirurgical Faculty of Maryland, Baltimore.

## TUESDAY MORNING, 9:30

*The Health and Safety Program of the U. S. Bureau of Mines*

Daniel Harrington, Chief, Health and Safety Branch, U. S. Bureau of Mines, Washington, D. C.

*The Public Health Interest in Industry—Federal, State and Local*

Warren F. Draper, M.D., Executive Officer, U. S. Public Health Service, Washington, D. C.

*Industrial Health Activities by Labor Departments in the Government*

Alice Hamilton, M.D., Consultant on Industrial Hygiene, Division of Labor Standards, U. S. Department of Labor, Washington, D. C.

*Independent Programs of Investigation and Prevention*

W. J. McConnell, M.D., Secretary Industrial Hygiene Section, American Public Health Association, New York.

## TUESDAY AFTERNOON, 2 O'CLOCK

*Industrial Surgery from the General Surgeon's Point of View*

Harry Mock, M.D., Chicago.

## SYMPOSIUM ON MEDICAL SERVICE TO SMALL INDUSTRIAL PLANTS

*Statement of the Problem*

Victor Heiser, M.D., and Donald Shafer, M.D., Consultants, Committee on Healthful Working Conditions, National Association of Manufacturers, New York.

*The Responsibility of the Private Practitioner*

Carey P. McCord, M.D., Director, Bureau of Industrial Hygiene, City of Detroit Department of Health, Detroit.

*Means for Accomplishment*

Glenn S. Everts, M.D., Melrose Park, Pa.

*Methods of Appraisal*

L. D. Bristol, M.D., Health Director, American Telephone and Telegraph Company, New York.

## HEARINGS BEFORE THE GRAND JURY IN WASHINGTON

The following additional witnesses, all of Washington, D. C. are reported to have appeared last week before the Special Grand Jury in Washington: Dr. Claude C. Caylor, associate professor of radiology, Georgetown University School of Medicine; Dr. John H. Lyons, Emergency Hospital; Dr. Charles S. White, professor of surgery, George Washington University School of Medicine, and Dr. Leon A. Martel, professor of gynecology, Georgetown University School of Medicine.

## RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company, entitled "Your Health," began Wednesday October 19 and will run consecutively for thirty-six weeks. The program is broadcast over the Blue network of the National Broadcasting Company each Wednesday at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).<sup>1</sup>

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

- December 7. Tuberculosis and the Teens.
- December 14. What Shall We Eat?
- December 21. Hidden Treasures in Foods.

1. Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.

## WOMAN'S AUXILIARY

## California

The auxiliary to the Alameda County Medical Association held a meeting October 21 with 100 members present. Mrs. Elizabeth Lossing of the Berkeley police department spoke on "Protective Work with Girls."

The auxiliary to the Orange County Medical Society met October 4 in Santa Ana. Dr. W. W. Roblee, president of the California Medical Association, gave an address on "Modern Trends in Medicine." Dr. Roblee urged members to study all bills and amendments pertaining to medical legislation.

September 17 the auxiliary to the Santa Clara County Medical Society held a social meeting at the home of Mrs. Russell V. Lee, on the campus of Stanford University, honoring Mrs. Clifford A. Wright, president of the state auxiliary. Mr. Clark Cypher, attorney, Palo Alto, discussed "The Humane Pound Act," which appeared as Proposition No. 2 on the ballot,

November 8.—On October 3 the auxiliary met at the Leon Ghetti Tea Room near Los Gatos. Mr. Adron Beene gave an address on "Medical Legislation."

## Mississippi

The auxiliary to the Mississippi State Medical Association is making an effort to acquaint the people of Mississippi with the purpose and the work of the Mississippi State Preventorium at Sanatorium. The auxiliary is sponsoring a statewide essay contest in the public schools of Mississippi. The subject of the essay is "The Preventorium."

## Oklahoma

Dr. L. S. Willour spoke on "The Basic Science Law" at a recent meeting of the auxiliary to the Pittsburgh County Medical Society in McAlester. The auxiliary presented a copy of "The Horse and Buggy Doctor," by Arthur E. Hertzler, to the public library.

## Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

### ARKANSAS

**Two Day Graduate Course.**—The Arkansas Medical Society conducted its fifth two day course of graduate instruction at the University of Arkansas School of Medicine in Little Rock October 12-13. The guest speakers were:

Dr. Leon Bromberg, St. Louis: Syphilis as a Problem in Differential Diagnosis; Present Status of Artificial Fever Therapy.  
Dr. James S. McLester, Birmingham, Ala.: The Newer Knowledge of Nephritis; Subclinical Deficiency Syndromes.  
Dr. Robert F. Short Jr., Dallas, Texas: Intestinal Obstruction; Problems of Surgery of the Right Upper Abdomen.

Among other speakers were Drs. Nicholas T. Hollis and Elizabeth D. Fletcher on "Insulin and Metrazol Shock in the Treatment of Dementia Praecox"; Carl A. Rosenbaum, "Technic for the Injection of Varicose Veins"; Jerome S. Levy, "Mode of Action and Uses of Sulfanilamide"; Ewell I. Thompson, "Scabies and Impetigo: Diagnosis and Treatment"; Robert Q. Patterson, "Tinea: Diagnosis and Treatment"; John N. Compton, "The Truth About Atabrine and Plasmochin," and Jesse D. Riley, State Sanatorium, "Diagnosis and Treatment of Tuberculosis by the General Practitioner."

### CALIFORNIA

**Changes in Health Officers.**—Dr. Morris Krutchkoff has been appointed health officer of Ferndale, succeeding Dr. Joseph M. Brown. Dr. Harold J. Shanks is now health officer of Pleasanton succeeding the late Dr. William D'Arcy Chace. Dr. Ellert E. Lundegaard, Weimar, has been appointed health officer of Colfax to succeed Dr. Ray C. Atkinson.

**Society News.**—Dr. Robert G. Majer, among others, discussed "Abdominal Symptoms in Hyperthyroidism" before the Los Angeles Surgical Society November 25.—A symposium on extrapulmonary tuberculosis was presented before the Trudeau Society of Los Angeles November 22 by Drs. Henry Sutherland-Campbell, David H. Kling, Herman Z. Semenov, Los Angeles, and Hubert T. Wilken, Santa Monica.

### CONNECTICUT

**Lectures on Gastro-Enterology.**—The Fairfield County Medical Association, cooperating with the local medical societies, is presenting monthly lectures on the gastrointestinal tract. Alfred Z. Gilman, Ph.D., New Haven, gave the first lecture in Danbury October 5 on "Mechanics of the Gastrointestinal Tract in Health and Disease." Dr. Zacharias Bercovitz, New York, gave the second, November 8, in Bridgeport, on "The Patient and His Indigestion." The remaining lectures will include:

Dr. John L. Kantor, New York, January 10, in Greenwich, Treatment of Peptic Ulcer and Its Complications.  
Dr. Samuel C. Harvey, New Haven, February 8, in Norwalk, Carcinoma of the Stomach.  
Dr. Isidor S. Ravdin, Philadelphia, March 14, in Stamford, Diseases of the Gallbladder and Bile Ducts.  
Dr. Chester M. Jones, Boston, May 11, in Danbury, Diseases of the Liver.

### ILLINOIS

**Hospital News.**—The cornerstone of the new building for St. John's Hospital was laid in Springfield October 16. The new unit will be twelve stories high with accommodations for 620 patients.

**Society News.**—Dr. Francis L. Lederer, Chicago, addressed the Rock Island County Medical Society in Moline November 8 on "Throat Complications of Interest to the General Practitioner."—Dr. Fred M. Drennan, Chicago, discussed "Diagnosis and Treatment of Irritable Colon" before the Will-Grundy County Medical Society in Joliet October 18. Dr. Jacob P. Greenhill, Chicago, addressed the society November 3 on "Diagnosis and Treatment of Obstetric Hemorrhages."—The McHenry County Medical Society was addressed October 27 by Dr. Philip H. Smith, Evanston, on "Management of Placenta Praevia."—A symposium on intestinal obstruction was presented before the Sangamon County Medical Society, Springfield, November 3 by Drs. Richard F. Herndon, Thomas D. Masters, David J. Lewis and Charles L. Patton, all of Springfield.

### Chicago

**Diphtheria at Hines Hospital.**—A quarantine was placed against the Veterans' Administration Facility in Hines November 27, closing it to visitors following an outbreak of four cases and one death from diphtheria, according to the *Chicago Tribune*. At the time of this report fourteen patients had infectious sore throats. It was stated that six diphtheria carriers were disclosed in the tests that were given to 1,200 staff members and 1,800 patients. The quarantine will be continued until danger of an epidemic is over.

**Dr. Black Appointed Acting President of Board of Health.**—Dr. Robert A. Black, professor of pediatrics, Loyola University School of Medicine, has been appointed president of the Chicago board of health. The appointment is temporary during the absence of Dr. Herman N. Bundesen, who has been granted leave of absence pending the outcome of the government's antitrust action against the milk industry, newspapers reported. Dr. Black has been a member of the board of health since 1935; he also is founder and superintendent of the La Rabida sanatorium in Jackson Park for children with heart disease.

### IOWA

**Annual Clinic.**—The State University of Iowa College of Medicine, Iowa City, presented its annual clinic November 10-11. The program covered fractures of the arm, head injuries and varicose ulcers. Dr. Harry P. Smith, Iowa City, was chairman of the committee on arrangements.

**State-Wide Survey of Gas Gangrene.**—A survey will be conducted in every county in the state by the fracture chairman and the president and secretary of each county medical society to obtain the history of every authentic case of gas gangrene in that county, according to the state medical journal. The work will be under the auspices of the fracture committee of the Iowa State Medical Society. Complete information will be obtained, including the name and age of the patient, the type of injury, whether or not prophylactic serum was given and when given; exact time gas developed; a positive bacterial finding of *Bacillus welchii*; time and exact type of treatment, and the final results showing mortality, duration of treatment, loss of limbs and duration of the disease.

### KANSAS

**Society News.**—At the meeting of the Kansas section of the American College of Physicians in Topeka November 4 the speakers included Drs. Philip W. Morgan, Emporia, on gastric acidity; Norman Reider, Topeka, headaches; Arthur J. Revell, Pittsburg, "Role of the Pituitary Gland in Clinical Medicine"; Frank A. Trump, Ottawa, "The Misuse of Digitalis"; Fred E. Angle, Kansas City, "Gallbladder Dysfunction"; Harold W. Palmer, Wichita, "Case of Acute Idiopathic Hematoporphyria with Acute Ascending Paralysis," and William C. Menninger, Topeka, "Cardiac Neuroses."

### KENTUCKY

**State Medical Election.**—Dr. John W. Scott, Lexington, was chosen president-elect of the Kentucky State Medical Association at the annual meeting in Louisville October 6. Vice presidents elected were Drs. James Duffy Hancock, Louisville; Ewing L. Palmore, Glasgow, and Joseph T. Molony, Covington. Dr. William E. Gardner, Louisville, was installed as president and Dr. Arthur T. McCormack, Louisville, was reelected secretary for a five year term. The 1939 meeting will be in Bowling Green.

**Dr. Abell Awarded Laetare Medal.**—Dr. Irvin Abell, Louisville, President of the American Medical Association and clinical professor of surgery, University of Louisville School of Medicine, was presented with the Laetare Medal of the University of Notre Dame, South Bend, Ind., at special ceremonies November 5. Most Rev. John A. Floersh, archbishop of Louisville, presided and Rev. John F. O'Hara, president of the university, made the presentation. The orator was Rev. Norbett Hoff, professor of philosophy at Notre Dame, and his subject "The Meaning of Leadership."

**New Superintendent of State Mental Hospital.**—Dr. Floyd K. Foley of the staff of the Veterans' Administration Facility, Lexington, has been appointed superintendent of the Eastern State Hospital, Lexington. He succeeds Dr. James L. Vallandigham, who resigned November 1. The change is in accordance with a law enacted at a special session of the state legislature last May with a view to reorganizing the state mental hospitals. As a part of the reorganization Dr. Joseph G. Wilson, formerly of the U. S. Public Health Service, was

appointed director of a new division of hospitals and mental hygiene in the state department of welfare at Frankfort. Appointment of Dr. Foley to the Lexington hospital was recommended by a committee of the Kentucky State Medical Association, according to newspaper reports. The committee included Drs. Arthur T. McCormack, secretary of the state medical association; Irvin Abell, President of the American Medical Association; William E. Gardner, president of the state association, and Arthur C. McCartv. all of Louisville; Ernest B. Bradley, Lexington; Austin Bell, Hopkinsville, and Carl C. Howard, Glasgow. Dr. Foley is a native of Kentucky and graduated from the University of Louisville School of Medicine in 1911. He has been associated with the Veterans' Administration since 1930 and on the staff of the facility at Lexington since 1933.

### MASSACHUSETTS

**Society News.**—The Hampden District Medical Society was addressed in Springfield October 25 by Dr. Henry R. Viets, Boston, on "Acute Lymphocytic Meningitis and Other Virus Diseases of the Central Nervous System."—The first fall meeting of the Worcester District Medical Society was addressed by Drs. Joseph M. Looney on "Determination of Serum Phosphatase and Its Clinical Significance"; James S. P. Beck, "Cause of Death in Newborn," and William G. Moran, "The Pathologist and His Relation to the General Practitioner." The society was addressed November 9 by Drs. Robert S. Palmer on "Bright's Disease and Hypertension" and Maurice B. Strauss, "Anemia: Modern Methods in Diagnosis and Treatment of Blood Dyscrasias." Both are from Boston.

### MINNESOTA

**Personal.**—Dr. Frank L. Jennings, assistant superintendent and associate medical director of Glen Lake Sanatorium, Oak Terrace, for twenty-one years, has been appointed superintendent and medical director of Sunnyside Sanatorium, Oaklandon, Ind., succeeding Dr. Argal E. Hubbard, it is reported. Dr. Jennings has been a clinical assistant professor of medicine at the University of Minnesota Medical School, Minneapolis; he is also a member of the board of trustees of the Hennepin County Tuberculosis Association.

**Society News.**—At a meeting of the Scott-Carver Medical Society in Montgomery October 11 Drs. George D. Eitel, Minneapolis, discussed "Traumatic Surgical Emergencies" and Ernest L. Meland, Minneapolis, urologic emergencies.—Dr. Hubert T. Sherman, Plainview, gave the presidential address before the seventieth annual meeting of the Wabasha County Medical Society in Wabasha October 6 on "Cooperation Within the Society"; other speakers included Drs. Gordon R. Kamman, St. Paul, "Epidemic Encephalitis"; Bernard A. Flesche, Lake City, "Granulocytopenia"; Edward Dyer Anderson, Minneapolis, "Practical Points in Pediatric Practice," and Walter C. Popp, Rochester, Minn., "Roentgen Therapy in Malignant Disease."—Dr. Raymond N. Bieter, St. Paul, discussed "The Chemistry and Therapeutic Use of Sulfanilamide" before the Washington County Medical Society October 11.

### MISSISSIPPI

**Baylor Faculty Members Address Central Society.**—Members of the faculty of Baylor University School of Medicine, Dallas, Texas, will present the program before the Central Medical Society in Jackson, December 6. The speakers will include:

- Dr. Calvin R. Hannah, Diagnosis and Management of Postoccipital Position and Toxemias of Pregnancy with Related Hypothyroidism.
- Dr. Henry M. Winans, Coronary Occlusion and Treatment of Hypertension.
- Dr. Hugh Leslie Moore, Pediatric Diagnosis and Common Allergic Disorders in Childhood.
- Dr. William B. Carrell, Fractures Involving the Ankle Joint and Osteomyelitis.
- Dr. Charles L. Martin, Developments in Treatment of Cancer with Radiation; A Study of Fallopian Tubes in Sterility.
- Dr. Alfred L. Folsom, Pyelitis in Children and in Pregnancy.
- Dr. Jesse Bedford Shelmire, The Handling of the Common Skin Diseases in Private Practice; Causes and Treatment of Eczema.

### MISSOURI

**Plan for Correlating Committee Activities.**—A plan for correlating committee activity in graduate instruction for physicians and health education for the public was effected by chairmen of the various committees of the Missouri State Medical Association at a meeting in St. Louis October 13. The chairmen of the following committees make up the new committee: graduate course, cancer, conservation of eyesight, fractures, health and public instruction, maternal welfare, medi-

cal economics, mental health, publication, physical therapy, and control of syphilis. The plan will not interfere with the activity of individual committees but will emphasize and control more concentrated discussions on specific subjects, from both lay and medical points of view.

### NEBRASKA

**Society News.**—Speakers before the Lancaster County Medical Society, Lincoln, October 4, were Drs. Hiram Winnett Orr, on "Prevention of Deformity in Arthritis" and Drs. Ephraim Korol and Harry A. Scott, "Etiology of Bronchiectasis."—Sioux City (Iowa) physicians addressed the Fire-Counties Medical Society (Cedar, Wayne, Thurston, Dixon and Dakota counties) in Wayne October 4 as follows: Drs. Jacob N. Lande on "Immunization"; Roy Crowder, "Perineal Repair"; Roland T. Rohwer, "Management of the Irritable Colon," and Howard I. Down, "Ulcers of the Stomach."—Dr. John F. Gardiner, Omaha, addressed the Madison Six County Medical Society, Norfolk, recently on "Recognition and Treatment of Some Endocrine Disorders."—Drs. Robert D. Schrock and Charles A. Owens, Omaha, addressed the Omaha-Douglas County Medical Society October 11 on "Diagnosis of Bone Tumors" and "Value of Heat Therapy in Sulfanilamide-Resistant Gonorrhea" respectively.

### NEW HAMPSHIRE

**Changes in State Board of Health.**—Dr. Charles A. Weaver, Concord and Manchester, has retired after more than twenty years of service with the state board of health as epidemiologist and director of venereal disease control. Dr. Weaver is 83 years old and graduated from the University of Vermont School of Medicine in 1881. Dr. John S. Wheeler, Wolfeboro, will take Dr. Weaver's place temporarily. Dr. Byron H. Farrall, Boscawon, director of the division of maternal and child health and crippled children services, has also resigned and has been succeeded by Dr. Mary Atchison, formerly of Dubuque, Iowa.

### NEW JERSEY

**Campaign Against Appendicitis.**—The Medical Society of New Jersey has begun its second annual campaign to reduce the appendicitis death rate in cooperation with pharmacists and school authorities. The society has sent 60,000 stickers to school physicians for distribution to students. The stickers bear a warning against taking laxatives in the presence of abdominal pain, advise calling the family doctor and explain that pain, cramps or soreness that lasts more than four hours is usually serious. Large placards with the same warning will be distributed to pharmacists, who will be asked to post them conspicuously.

**Society News.**—Dr. William T. Lemmon, Philadelphia, addressed the Gloucester County Medical Society, Woodbury, September 15 on "Surgery of the Sympathetic System."—Drs. Edward G. Waters, Jersey City, and Theodore Neustaedter, New York, addressed the Passaic County Medical Society, Paterson, September 8, on "Injuries to the Birth Tract During Parturition" and "Modern Concept of the Relationship and Value of Endocrines in Obstetrics" respectively.—Dr. Leonard Averett, Philadelphia, addressed the Atlantic County Medical Society October 14 on "Advantages of the Vaginal Operative Approach to Pelvic Pathology Over the Abdominal Route" and Dr. Watson B. Morris, Springfield, "Objectives and Administrative Policies of the Medical Society of New Jersey."—Dr. Howard C. Taylor Jr., New York, lectured at Aurora Institute, Morristown, November 6, on ovarian and pituitary therapy.

### NEW YORK

**Albany Alumni Meeting.**—The Alumni Association of Albany Medical College held its annual Alumni Day December 1 with Dr. Frank H. Lahey, Boston, as the guest speaker on "Newer Surgical Entities." Both operative and dry clinics were presented at the hospital. In the afternoon there were teaching demonstrations in the college.

**Changes in State Health Department.**—Dr. Ernest L. Stebbins has been made assistant commissioner of the state department of health in charge of preventable diseases, the department announces. Dr. James E. Perkins is now director of communicable diseases and Dr. Paul A. Lembcke epidemiologist in the division of communicable diseases. The following have been appointed district health officers in the districts indicated: Drs. Samuel A. Hyman, Buffalo, to the Utica dis-

trict; Franklyn B. Amos, Batavia, to the Amsterdam district; Harry L. Chant, Kingston, the Middletown district, and Hollis S. Ingraham, Albany, the Kingston district. Dr. Frank E. Coughlin, Albany, has been promoted to the position of district state health director in charge of the eastern districts.

#### New York City

**Annual Hospital Fund Drive.**—The United Hospital Fund is conducting its annual drive for funds to carry on the work of the ninety-two voluntary hospitals associated with the fund. A minimum of \$2,523,179 is needed, it was announced. Mr. Colby M. Chester is chairman of the campaign.

**Tuberculosis Conference.**—A clinical session on chronic pulmonary diseases under the auspices of the Tuberculosis Sanatorium Conference of Metropolitan New York will be held at Cornell University Medical College December 14. The speakers will be Drs. Ida Levine, on "Bilateral Simultaneous Pneumothorax"; Abraham V. Shapiro and Foster Murray, "Clinical Application of Tomography to the Study of Pulmonary Tuberculosis," and Daniel A. Mulvihill, "Late Results of Apicolytic Thoracoplasties."

**Society News.**—Dr. Ira Cohen addressed the New York Surgical Society October 19 on "Acute Epidural Spinal Infection."—Drs. Foster Kennedy, Emanuel D. Friedman and Orman C. Perkins addressed the Association for the Advancement of Industrial Medicine and Surgery October 19 on "Head Injuries."—A symposium on macrocytic anemias was presented at a meeting of the Medical Society of the County of New York October 24 by Drs. George R. Minot, Boston; Cornelius P. Rhoads, New York; Maurice B. Strauss, Boston, and Cyrus C. Sturgis, Ann Arbor, Mich. The program was arranged in conjunction with the Graduate Fortnight of the New York Academy of Medicine.

**Expansion of Kings County Hospital.**—The city planning commission has included in its budget funds for expansion of Kings County Hospital, Brooklyn, on a large scale, the department of hospitals announced November 3. The items approved include a building for chronic patients, \$2,735,500; a building for patients with mental or emotional disturbances requiring temporary diagnostic facilities, \$1,430,000; a building to relieve overcrowding in the clinics, \$1,087,500, and a central hospital laboratory \$400,000. Although the hospital's capacity has been reduced by 275 beds during the past year by demolition of the old main building, the hospital population was 2.5 per cent larger than in 1937, it was reported.

**Medical-Dental Meeting.**—The eighth annual medical-dental convention arranged by the Joint Committee of the Organized Medical and Dental Professions of New York will be held December 5 at the Hotel Pennsylvania. Papers will be presented at the morning session by the following:

Theodor Rosebury, D.D.S., Primary and Secondary Factors in Dental Caries in Animals and Man.

Thomas A. Cook, D.D.S., Oral Infections: Factors That Influence the Diagnosis and Treatment.

Dr. Nathan Rosenthal, Lesions of the Oral Mucous Membranes in the Various Types of Blood Dyscrasias.

Dr. Walter F. Watton, The Pediatrician's Role in Prevention of Caries.

A clinical session will be held in the afternoon, when cases will be shown from Long Island College of Medicine, Cornell University Medical College and Mount Sinai Hospital.

#### NORTH CAROLINA

**Personal.**—Dr. David E. Plummer, Mocksville, has been appointed to take charge of a venereal disease clinic in Durham, a full time position.—Dr. Albert F. Houck, Lenoir, has presented his medical library to the Caldwell County public library, where a special section will be set aside for it.

**Society News.**—Dr. Porter P. Vinson, Richmond, Va., addressed the Forsyth County Medical Society, Winston-Salem, October 11 on bronchoscopy.—Dr. John P. Peters, New Haven, Conn., addressed the Buncombe County Medical Society, Asheville, October 14 on "Clinical Problems in Salt and Water Metabolism." Dr. John T. Saunders addressed the society October 3 on "Common Functional Foot Disorders."

#### OHIO

**Joint Obstetric Meeting.**—Obstetricians of Pittsburgh and Buffalo were guests of the obstetric and gynecologic section of the Cleveland Academy of Medicine November 7. Clinics, demonstrations and discussions were held at MacDonald House and St. Luke's Hospital during the day and in the evening Dr. William E. Caldwell, New York, gave an address on "X-Ray Pelvimetry."

**Annual Lecture Course in Lima.**—Drs. Carl E. Badgley, Ann Arbor, Mich., and Charles A. Doan, Columbus, conducted the annual postgraduate course sponsored by the Academy of Medicine of Lima and Allen County September 22-27. Dr. Badgley discussed pain low in the back, ununited fractures, epiphyseal fractures of the elbow joint and soft tissue lesions of the upper extremities. Dr. Doan's subjects were iron metabolism and the simple anemic states, macrocytic anemias, the splenopathies, role of the white blood cells, the lymphadenopathies and new approaches to recognition and control of the leukemic states.

**Conference on Legislative Activities.**—A conference of legislative committeemen and officers of county medical societies was held in Columbus October 2. Dr. Daniel C. Houser, Urbana, chairman of the subcommittee on legislation of the Ohio State Medical Association, presided. The chief speakers were Drs. Roscoe L. Sensenich, South Bend, Ind., a Trustee of the American Medical Association; Barney J. Hein, Toledo, president of the state association; Louis Howard Schriver, Cincinnati, councilor of the first district; Carl W. Sawyer, Marion, a member of the subcommittee on legislation, and Mr. Charles S. Nelson, executive secretary.

#### PENNSYLVANIA

**Hospital News.**—Allentown Hospital recently opened a plastic surgery clinic under the direction of Dr. Kerwin M. Marcks, Emaus.

**County Society Graduate Lectures.**—The Butler County Medical Society sponsored a series of lectures at the Butler County Memorial Hospital, Butler, October 13 to November 19. The series was arranged by the committee on graduate education of the Medical Society of the State of Pennsylvania. Following was the schedule:

Dr. Roy W. Scott, Cleveland, Diagnosis and Management of the Common Types of Cardiovascular Disease.

Dr. Edward Weiss, Philadelphia, Diseases of the Kidney.

Dr. Harry E. Bacon, Philadelphia, Diagnosis and Treatment of the More Common Pathologic Conditions of the Anus, Rectum and Colon.

Dr. Arthur J. Skeel, Cleveland, Practical Aids and Procedures in the Field of Obstetrics.

Dr. Harold L. Mitchell, Pittsburgh, Neurological Diseases—Emphasizing the Neuroses.

Dr. Richard A. Kern, Philadelphia, Allergy—Demonstration of Diagnostic Procedures.

#### Philadelphia

**Tuberculosis Conference.**—The annual Philadelphia Tuberculosis Conference was held November 15 at the Bellevue-Stratford under the auspices of the Philadelphia Health Council and Tuberculosis Committee. Dr. John Alexander, Ann Arbor, Mich., addressed a luncheon meeting on "Relation of Collapse Therapy to the Control of Tuberculosis" and a medical session in the evening on "Role of Lobectomy and Pneumonectomy in Management of Tuberculosis."

**Dr. Bond Resigns Hospital Posts.**—Dr. Earl D. Bond, director of the Institute for Mental Hygiene of the Pennsylvania Hospital and head of the department of nervous diseases at the hospital, has resigned from these positions to devote his time to research, it is reported. He will be succeeded by Dr. Lauren H. Smith, a member of the executive staff of both units since 1926. Dr. Bond will continue as vice dean for psychiatry and professor of psychiatry at the University of Pennsylvania Graduate School of Medicine.

#### WASHINGTON

**Northwest Orthopedic Society.**—The annual meeting of the Pacific Northwest Orthopedic Society was held in Tacoma October 1. The following officers were elected: Drs. Donald M. Meekison, Vancouver, B. C., president; Donald A. Murray, Seattle, vice president, and John R. Naden, Vancouver, secretary.

**Committee on Industrial Health.**—Dr. Hubbard T. Buckner, Seattle, has been made chairman of a new committee on industrial health, appointed by the president of the Washington State Medical Association, Dr. Harry E. Rhodehamel, Spokane. Other members of the committee are Drs. Samuel L. Caldbick, Everett, and Richard J. Bailey, Spokane.

#### WEST VIRGINIA

**More Diseases Made Reportable.**—The state Public Health Council at a meeting October 31 in Bluefield passed a regulation requiring that pneumonia, typhus fever, undulant fever and diarrhea of the newborn be reported by physicians. The rule went into effect November 1.



**The Schwinn Lecture.**—Dr. Howard R. Sauder, Wheeling, gave the annual Schwinn Lecture of the Ohio County Medical Society, Wheeling, November 11. His subject was "The Clinical Variants of Coronary Arteriosclerosis." The Schwinn lecture honors Dr. Jacob Schwinn, long a member of the society and now 84 years old.

**Society News.**—Drs. Alfred Spates Brady Jr. and Russel Kessel, Charleston, addressed the Logan County Medical Society recently on "Management of Congestive Heart Failure" and "Treatment of Artificial Menopause" respectively. —The annual joint meeting of the Preston and Monongalia county medical societies was held in Hopemont recently with Dr. Ray M. Bobbitt, Huntington, as the speaker, on "Medical Management of Urinary Tract Infections." —Dr. Robert V. Funsten, Charlottesville, Va., addressed the Ohio County Medical Society October 14 on "Some Problems in Fracture Treatment."

### WISCONSIN

**District Meetings.**—The Tenth Councilor District of the State Medical Society of Wisconsin held a meeting September 29 in Eau Claire with the following speakers: Drs. Jennings C. Litzenberg, Minneapolis, on "Toxemias of Pregnancy"; William S. Middleton, Madison, "Anemias, Their Interpretation and Treatment"; Carl W. Waldron, Minneapolis, "Fractures of the Face and Jaw," and Fred S. Cook, Eau Claire, "Foreign Bodies in the Food and Air Passages." —The Eleventh Councilor District met in Superior recently in conjunction with the Interurban Academy of Medicine. The speakers were Drs. Francis D. Murphy, Milwaukee, on cardiac disease; James C. Sargent, Milwaukee, conservative surgery of the kidney; Robert E. Burns, Madison, orthopedic surgery; John E. Gonce Jr., Madison, abdominal disease in children, and Raymond G. Arveson, Frederic, adequacy of medical care in Wisconsin.

### GENERAL

**Meeting of Anesthetists.**—The annual meeting of the American Society of Anesthetists will be held December 8 at the building of the College of Physicians of Philadelphia. The speakers will be Drs. Lincoln F. Sise, Boston, on "A Pioneer's Conception of Anesthesia as a Specialty for the Young Physician of Today" and Ralph M. Waters, Madison, Wis., "The Management of the Anesthetic Period as a Means of Preventing Undesirable Effects During Convalescence." Dr. Paul M. Wood, New York, is secretary of the society.

**Warning of Swindler.**—Illinois physicians have complained that a man claiming to represent "Westcot and Company" or "Sherman and Company" of Chicago has taken orders for surgical supplies, collected for them at the time and failed to deliver the goods. Letters sent by these physicians to the addresses given for these concerns have been returned with the notation "No such address" and the firms were not listed in the Chicago telephone directory. The impostor was described as being from 45 to 55 years old, 5 feet 8 inches tall, weighing about 135 pounds and having light brown hair and smooth face. In one instance he gave his name as "Mr. Westcot."

**Index for Psychologic Literature.**—The American Psychological Association recently appointed an advisory committee to supervise the compilation of the Psychological Index now under way with the assistance of the Works Progress Administration. Albert T. Poffenberger Jr., Ph.D., of Columbia University is chairman of the committee and the members are Karl M. Dallenbach, Ph.D., Cornell University, Ithaca, N. Y.; Chauncey M. Louttit, Ph.D., Indiana University, Bloomington, and Raymond R. Willoughby, Ph.D., Brown University, Providence, R. I. The committee will advise in the direction of the project and assume responsibility for all decisions pertaining to the actual index and for psychologic nomenclature, it was said.

**Fellowships Available in Medical Sciences.**—Fellowships in the medical sciences, administered by the Medical Fellowship Board of the National Research Council, of which Dr. Francis G. Blake of Yale University is chairman, will be available for the year beginning July 1, 1939. These fellowships are open to citizens of the United States and of Canada who possess an M.D. or a Ph.D. degree. They are intended for recent graduates and not for persons already established. Fellows will be appointed at a meeting of the Medical Fellowship Board about March 1. Applications to receive consideration at this meeting must be filed on or before Jan. 1, 1939. Appointments may begin on any date determined

by the board. For further particulars concerning these fellowships, address the secretary of the Medical Fellowship Board, National Research Council, 2101 Constitution Avenue, Washington, D. C.

**International Neurological Congress in 1939.**—The Third International Neurological Congress will be held in Copenhagen, Denmark, Aug. 21-25, 1939, under the presidency of Prof. Viggo Christensen. Three days of the congress will be devoted to the following symposiums: "The Autonomic Nervous System with Special Reference to the Endocrine System," "Heredofamilial Disease, Especially from the Genetic Aspect" and "Neurological Aspects of the Avitaminoses." One day will be given over to ten minute papers by active members of the congress. Those desiring to present such papers must furnish to the secretary for the United States a title and an abstract of not more than 200 words on or before March 1, 1939. The committee for the United States will tentatively accept the papers and forward them to the Danish committee for final action. Proposers of papers will probably be notified about May 1, 1939, whether the papers have been accepted. Membership in the congress will be comprised of active and associate members. Applicants for active membership must belong to some national or local neurologic, psychiatric or neuropsychiatric association or society and must have an endorsement of their applications by the local association or by some neurologist or psychiatrist known to the United States committee. The fee for active membership is \$8. Members of families, physicians in other specialties and nonmedical persons engaged in related fields of activity may apply for associate membership, the fee for which is \$4. The American Express Company is the official travel agent. The members of the United States committee are Drs. Bernard Sachs, New York, chairman; Henry Alsop Riley, New York, secretary; Foster Kennedy, New York; John F. Fulton, New Haven, Conn.; Stephen W. Ranson, New York, and Stanley Cobb, Boston. Dr. Riley's address is 117 East Seventy-Second Street, New York. Canadians interested in attending should communicate with Dr. Wilder G. Penfield, 3801 University Street, Montreal, Que.

**Review of Causes of Death.**—The U. S. Bureau of the Census recently issued a detailed tabulation of deaths that occurred in the United States in 1936 by sex, race and age. Included in the report was a table showing the number of deaths and the death rate each year since 1900, when the original death registration area was established. Over the span of years the rate has decreased from 17.6 to 11.5. Originally the registration area contained only ten states; since 1933 statistics have been collected from all states. Diseases of the circulatory system caused the greatest number of deaths in any large group. Among specific causes were chronic myocarditis and myocardial degeneration 110,654, chronic endocarditis 50,529, disease of the coronary arteries 48,622 and angina pectoris 17,760. Cancer and tumors caused 149,126 deaths, with most numerous group being cancer of the digestive tract, 68,239 deaths. Cancer of the uterus caused 16,280 deaths. Infectious and parasitic diseases caused 148,798 deaths. Included in this group were 3,098 from typhoid, 22,889 from influenza, 3,020 from epidemic cerebrospinal meningitis, 71,527 from tuberculosis and 12,612 from syphilis. There were thirty-five deaths from smallpox. Diabetes, included in a miscellaneous group, were caused 30,406 deaths. Diseases of the nervous system were responsible for 143,543 deaths, of which 103,560 were attributed to cerebral hemorrhage. Another large group is diseases of the respiratory system, which caused 134,920 deaths. Of these 119,055 were listed under pneumonia. Notable in the classification of diseases of the digestive system were appendicitis with 16,480 deaths and cirrhosis of the liver with 10,587. Ulcer of the stomach caused 5,987. Violent and accidental deaths accounted for 138,775 persons. There were 18,294 suicides, 13,522 of them among men; firearms were used in 6,771 cases. There were 10,232 homicides. Lives lost in automobile accidents amounted to 35,761; in addition, 1,697 persons died in railroad and automobile collisions and 269 in street car and automobile collisions. There were 26,673 deaths from injuries received in falls, 6,973 from drowning, 6,793 from burns and 1,807 from accidental gas poisoning.

### Deaths in Other Countries

Sir James Barr, vice president of the British Medical Association and for many years a leader in prison reform, died in London November 16, aged 89. —Dr. Jane H. Walker, who is said to have been the first physician to introduce the open air treatment of tuberculosis in England, died in London November 17, aged 79.

## Foreign Letters

### LONDON

(From Our Regular Correspondent)

Nov. 5, 1938.

#### Radium Therapy

The report of the Radium Institute for 1937, which has just been published, shows the progress which has been made during the year.

##### CARCINOMA OF THE CERVIX UTERI

The technic has been altered by increasing the content of the uterine applicator; the most distal tube has been raised from 10 to 15 mg., the other two tubes remaining at 10 Gm. Thus the total dose is increased to 9,120 mg. hours. One of the complications considered is invasion of the urinary bladder. Mic-turition symptoms and bimanual palpation were found to be unreliable indications of this. It had been suggested that, when the bladder is definitely involved by a growth, only local and palliative treatment should be given and that cystoscopy is a means of picking out cases not worth treating from a curative point of view. The series of cases now under review does not support this view. Several patients who were considered to have cancer of stage 4 have lived long enough without disease to have warranted full treatment. Recurrences after Wertheim's operation have been found to be worth treating by radiation. Of eighty patients treated between 1925 and 1932, ten survived five years and more, twelve were untraced and one died from other causes. Since 1932, five patients have been treated, of whom three are alive. All these were treated either by vaginal irradiation alone or by this combined with interstitial irradiation to a recurrent mass carried out through the vagina.

##### LIMBAL TUMORS

Good results were obtained in the irradiation of limbal tumors (growths at the junction of the cornea and conjunctiva, most of which are squamous cell epithelioma). There were twenty-eight cases, in most of which contact irradiation was given with unscreened radium for from fifty to sixty minutes. Two further exposures were given at intervals of from six to eight weeks. No case of postirradiation cataract occurred. It has been found that this sequel is confined to treatment by gamma radiation with screened radium for long periods.

##### PITCH WARTS

A large number of cases of pitch warts were treated. These are very common in those who work with gas, tar, pitch and the various oils which are derived from the destructive distillation of coal. They also occur in those who work with the various creosote and anthracene oils. Excepting the scrotum, pitch warts occur on exposed parts of the body—the face, neck, scalp, hands and forearms. They take two forms: the soft villous type, which bleeds easily, and the hard, smooth rounded variety, which is the more common. The latter can often be detected by palpation before they become visible. They then appear as separate conical warts with a black center, usually depressed. If ulceration occurs, it affects only the apex. The importance of pitch warts lies in the fact that if neglected they may develop into epitheliomas. Their prompt removal in the precancerous stage is therefore indicated. Education of the workers in habits of cleanliness and the reporting of any suggestive lesion have reduced the incidence and promoted early treatment. Pitch warts are extremely radiosensitive. They are treated by unscreened radium in flat applicators containing 5 mg. per square centimeter. These are placed in contact with the wart for periods of from eighty to 100 minutes. In almost every case the warts disappear in four or five weeks. In only four of 100 cases was a second application necessary. In only three

cases was the lesion malignant. Two lesions were treated by excision. One, on the forearm, was treated by radon seeds and disappeared. A secondary gland appeared in the axilla three months later and was treated by surface radium. The patient had no further trouble.

### PARIS

(From Our Regular Correspondent)

Nov. 5, 1938.

#### Birth Rate a Source of Great Anxiety to France

If the present drop in the national birth rate continues, the population of France in fifty years will drop from 40,000,000 to 28,000,000. Deaths exceeded births by 14,000 in 1937, when foreigners were included in the tabulation, and by 30,000 for French families alone. The national birth rate in 1876 was more than 1,000,000, as compared with 616,000 in 1937. During this period the average duration of life has increased from forty-five to sixty years. At the present rate France will lose 100,000 inhabitants a year and in another twenty years the loss will reach 200,000 a year. Meanwhile, in the totalitarian states the birth rate is rapidly increasing. There were 861,000 more births than deaths in 1937 in Italy.

#### French Surgical Congress

The third subject chosen for special reports and discussion at the French Surgical Congress was sarcomas of the muscles and intermuscular septums of the extremities. The reporters were Drs. Moulouquet of Paris and Pollosson of Lyons. The reports included an analysis of 119 personally observed cases; the condition had arisen in the intermuscular fibrous tissue in forty-three cases and in the muscles in thirty-seven. Sarcoma of the latter type is encapsulated and hence easily enucleated, but the capsule is so thin that invasion of the adjacent tissues is frequently observed in the recurrences following removal. Although the vessels and nerves are usually simply displaced, they may be so adherent as to render separation impossible. The older teaching that regional involvement of lymph nodes is rare must be changed in view of recent experiences. As to sarcoma of the muscles, there are two distinct forms: first, an encapsulated form, the capsule, however, being so thin that local recurrence is often observed after apparently easy enucleation, and second, an infiltrating form, in which the sarcoma invades the muscle in a diffuse manner but may be limited to the particular muscle for some time. This may explain why in some cases cure has followed excision of a single muscle.

In addition to the sarcomas arising in the intermuscular septums and muscles, other types are found, such as bone-forming tumors in the muscular tissue, i. e. osteoblastic sarcomas; also sarcoma of the aponeurosis, and myxoid fibrocytomas. Pulmonary metastases are the most common, having been found in twenty-nine of the 119 cases. Microscopically, one observes various types, such as (a) the type with undifferentiated structure, eight cases; (b) the fibroblastic type, thirty-eight cases, in only five of which was the patient alive three years after operation; (c) the lipoblastic type, thirty-three cases, with only five three year cures in twenty-six cases; (d) the rhabdoblasic type, which is also very malignant, thirteen cases; (e) the osteoblastic type, which is extremely malignant, and (f) the angio-blastic type, either pure or mixed.

The prognosis in general is unfavorable; only fifteen apparent (three year) cures were observed in 119 cases. The duration of life without operation is, on an average, two or three years; hence operation is justifiable. If exploration reveals a well encapsulated tumor, it should be removed. If there is no such encapsulation, the choice lies between amputation and irradiation. The latter offers a prospect of cure if the microscopic study reveals the existence of types like the undifferentiated or embryonal tissue form, or the osteoblastic, because they are radiosensitive. If a fair trial of irradiation for these two types shows no decrease in the size of the tumor, only amputation

can be considered. For all other types surgical intervention is indicated, e. g. disarticulation at the hip or shoulder or even a more radical operation.

The discussion was opened by Mr. Gordon Taylor of London, who had collected sixty-two cases of sarcoma of the muscles, nineteen of which were personally observed. The use of radium had given disappointing results. In some cases high voltage roentgen therapy was very successful, but in spite of an occasional good result Mr. Taylor agreed with Drs. Moulouguet and Pollosson that only radical surgical measures were indicated. This was also the opinion of Professor Tixier of Lyons after a trial of all other methods of treatment. Dr. Antoine Bécère of Paris believed that it was advisable to irradiate in all cases, because, although about 30 per cent of the sarcomas are radio-sensitive, it is impossible in advance to judge which are radio-sensitive. If the tumor decreased in size after irradiation, the operative intervention could be carried out in a less radical manner and the end results would not be changed, because irradiation had been employed.

#### OTHER PAPERS

Dr. Robert Mondor made a plea for early intervention in cancer of the lung. The majority of cancers were primary in the bronchi, and the chances for a favorable result depended on an early diagnosis. Operative intervention was indicated because irradiation was of no avail. The diagnostic signs were seldom clearcut; hence bronchoscopic examination, biopsy and search for the characteristic cells in the sputum must not be delayed. A round shadow was seen as often with pulmonary echinococci as with cancer. Exploratory thoracotomy merited being employed far more frequently than it had been in the past. In two cases favorable conditions for operation existed; one patient shows no signs of recurrence two and a half years after operation, but the other died of acute pulmonary edema as a post-operative complication. As favorable conditions for operation Dr. Mondor regarded localization to one lobe, absence of adhesions, no evidence of extension to the hilus, pleura or diaphragm and absence of infection.

Dr. Pascalis of Paris warmly endorsed the plea for exploratory pleurotomy, which is not followed by any serious complications provided an artificial pneumothorax has been established as a preliminary measure.

Drs. Loubat and Magendie of Bordeaux in a paper on prevention of new bone formation after thoracoplasty recommended a 20 per cent solution of tannic acid as being far superior to solution of formaldehyde. In thirty cases they found that regeneration of bone, which is such an unwelcome complication of thoracoplasty, had usually been completely inhibited. Even when the measure was only partially successful, the new bone formation occurred so late as to play an important part.

Prof. Raymond Grégoire and Dr. Claude Bécère read a paper on uterine hemorrhages from endocrine disturbances. An abstract of a similar communication by Dr. Bécère appeared in THE JOURNAL October 22, page 1603. The authors recommended the use of hysterosalpingography in the diagnosis of chronic adnexal lesions, which are the most common source of uterine bleeding in the absence of lesions of the uterus. This method of diagnosis permits immediate exclusion of uterine causes of bleeding and early recognition of a hydrosalpinx as distinguished from salpingitis of infectious origin. The latter should be treated conservatively, but operation is indicated for hydrosalpinx.

#### Prof. Jules Bordet Honored

One of the highest honors which the French government can bestow on those who have made noteworthy contributions to the welfare of the human race was recently conferred on Prof. Jules Bordet, director of the Pasteur Institute of Brussels. This honor is a recognition of the work of Professor Bordet

in the science of immunology, which has also merited his being awarded the Nobel prize in medicine. At a recent meeting of microbiologists at the Pasteur Institute of Paris, Professor Martin, director of the institute here, conferred the insignia of the grand cross of the Legion of Honor on Professor Bordet on behalf of the French government.

#### BERLIN

(From Our Regular Correspondent)

Oct. 24, 1938.

#### Measurement of the Caliber of Retinal Vessels

Investigations of hypertensive and kidney disease have disclosed that for pathologic study of these disorders the condition of the arterioles, especially with respect to the width, is of significance. The only arterioles which can be observed directly are the arteries of the retina. (With their diameters of 0.1 mm. they are to be regarded as arterioles.) For evaluation of the caliber of the retinal arteries one has hitherto, *faute de mieux*, been content with a single measurement. One must consider that in myopic eyes the retinal vessels appear for optical reasons as narrower and in hyperopic eyes, on the contrary, wider. Accordingly, in taking the measurement one compares the breadth of the retinal vessels in the ophthalmoscopic picture with the diameter of the optic papilla. Attempts at more accurate mensuration have heretofore been without satisfactory results; the reason for this is that even with the maximal attention on the part of both examiner and patient the influence of minute movements could not be excluded. Therefore exact results could not be elicited by measurement with a micrometer scale, and the most accurate procedure was a measurement based on photographs of the fundus oculi.

Professor Lobeck of Jena has recently succeeded, by means of a new method, in avoiding all sources of error. If a new measuring apparatus, of his own invention, is used, only a single reading is necessary instead of the customary two readings. This device enables one in a simpler manner and in an extremely brief time (from one to two minutes) to obtain precise measurement of the caliber of vessels of the fundus oculi, and it thus creates a sound basis for conclusions relative to the pathology of kidney disease and hypertensive disorders. The new method depends on adaptation of the principle of doubling, the so-called heliometric principle, in a somewhat modified form, to the ocular of a Gullstrand ophthalmoscope of the so-called simplified type. This ocular, known as the measuring ocular, was manufactured by the Zeiss firm of Jena according to Professor Lobeck's specifications; it permits exact measurements of vascular diameter and papillary diameter to be made under identical optical conditions and thus provides good comparable values. Such results were formerly impossible, since the heliometer principle was applied not to the ocular of Gullstrand's ophthalmoscope but to the ophthalmoscopic lens which was turned toward the eye of the patient.

The new method of measuring is completely uninfluenced by any involuntary movement of the examined eye, since it is a question of only one examination. Use of this new method for measurement of the calibers of the retinal vessels and papillary border have led to the following observations: In red hypertension the values are exactly the same as in health; in pale hypertension there is an obvious contraction of the retinal arteries, and there is an even greater contraction in cases of genuine chronic interstitial nephritis. Conversely, in all three of the disorders the diameters of the retinal veins present normal values. Measurement of the caliber of the retinal arteries thus enables one to establish for the hypertensive patient a differential diagnosis of red hypertension, pale hypertension or true chronic interstitial nephritis.

In renal disorders too the retinal arteries present various measurements, whereas the venous diameters always approximate those observed in healthy subjects. In acute nephritis as

well as in nephrosis the arteries of the papillary borders are observed to be of normal width, but in chronic nephritis they are plainly contracted. Conversely, the venous diameters exhibit no narrowing. The arterial contraction is still more marked in secondary chronic interstitial nephritis but is not so pronounced as in true chronic interstitial nephritis. In retinitis albuminurica the arteries are markedly contracted if the basis is chronic interstitial nephritis and less pronounced if the basis is secondary chronic interstitial nephritis; these observations too may be of diagnostic importance.

#### Radical Operation for Mammary Cancer

Dr. O. Thies recently discussed the surgical therapy of mammary cancer in use at the surgical clinic of Tübingen University. Of greatest importance in the treatment of mammary cancer is a knowledge of the routes of metastasis into secondary tumors. It has become questionable whether the blood or the lymphatics are of the greater significance. Frequently when the cancer appears little advanced as yet according to palpation of the axillary lymph nodes, the surgeon encounters keen disappointment because of the manifestation of remote metastases following radical operation. Thies was able to determine metastases in the regional lymphatics on microscopic serial examination in 100 cases of mammary carcinoma. It was remarked how often confusion of inflammatory changes with metastases and the reverse proved a source of serious error. Frequently histologic examination of the smallest lymph nodes would disclose widespread metastases, whereas clinically prior to and at operation no metastatic sites were encountered. In follow-ups of the patients, complete correspondence was evidenced between the prognosis based on tissue studies and the further course. Not only was the importance of the lymphatics in the metastasis of carcinoma again corroborated, the value and suitability of radical operation was also established. The latter should include removal of the pectoralis minor muscle.

#### Professor von Noorden 80 Years Old

Carl von Noorden celebrated his eightieth birthday September 13. A pupil of Riegel and Gerhardt, Noorden was from 1894 to 1906 director of the internal medical section of the municipal hospital at Frankfort on the Main. He then went to Vienna to succeed Nothnagel as ordinarius in internal medicine. In 1913 he returned again to Frankfort, there to direct a private clinic. In 1929 he accepted a call from the city of Vienna to serve as consultant to the municipal hospitals on disorders of metabolism and nutrition as well as dietetics. Preeminently a clinician, von Noorden contributed to numerous domains of internal medicine, especially to the knowledge of the pathologic and clinical aspects of metabolic disorders such as diabetes, diseases of the kidney, the anemias, obesity, and intestinal disorders. He is the author of several well known monographs on these conditions. His book on diabetes, "Die Zuckerkrankheit und ihre Behandlung" (the later editions of which were written in collaboration with Isaac) and the manual for diabetic patients, "Verordnungsbuch und diätetischer Leitfaden für Zuckerkrankhe," of which Isaac was likewise co-author, are widely used and have passed through numerous editions.

#### Prof. Dr. Edgar Atzler Is Dead

Prof. Dr. Edgar Atzler, director of the Kaiser Wilhelm Institute of Occupational Physiology, Dortmund, is dead at the early age of 50. Atzler may be called the founder of present day occupational physiology. He founded the institute in 1929 after having directed a smaller similar institution in Berlin for some years. Atzler published much that was fundamental to his chosen field, including studies of the anatomy and physiology of work, the interrelation of nutrition and working capacity and the suitability of industrial apparatus. In addition he published a textbook "The Body and Work" and founded the journal *Arbeitsphysiologie*. It has already been possible to turn a good part of the results of his investigations to practical account.

#### BUDAPEST

(From Our Regular Correspondent)

Oct. 15, 1938.

#### Electrical Shock

Dr. Kormoczi, senior physician to and for thirty years in the service of the Budapest Ambulance Society, says that to resuscitate a patient following an electrical accident first aid should be given on the spot by the immediate application of artificial respiration. Professor Jellinek, lecturer on electrical accidents, protested against the belief of some physicians that a period of from five to eight minutes between the cessation of respiration and the commencement of artificial respiration is of no special importance. In Kormoczi's experience the very first minutes are most important and decisive. Artificial respiration should be applied in every instance.

#### Prof. Tiborius Györi

Medical science mourns the loss of Tiborius Györi, professor of medical history at Budapest University. Györi graduated in 1894 and Budapest University sent him to Düsseldorf, Germany, in 1898 to study the medical history exhibition there. He knew not only German but also French, Italian, Latin and Greek. He spent weeks studying the exhibits and decided there to devote his life to medical history. During the years 1898-1900 he wrote thirteen historical treatises and two large historical works. After finishing a book on Hungarian medical bibliography he undertook to answer the question: What was the epidemic disease which appeared in the sixteenth to eighteenth centuries in Hungary and spread through Vienna to Germany and the Netherlands and was then called morbus Hungaricus? He collected data from seventy-four original publications, from which he concluded that morbus Hungaricus was exanthematous typhus. His work became known to Germany and in 1898 the medicohistorical part of Virchow's Jahresbericht der gesamten Medizin was written in part by him. In 1900 Györi became lecturer to the Budapest University on medical history. He undertook to investigate the family tree of Ignatz Semmelweis, to prove that the latter was Hungarian. He gave a memorial address on Semmelweis at the Royal Medical Society's festival in 1909 and shortly afterward at the Semmelweis memorial festival of the university. It was his idea to issue a stamp to popularize the memory of Semmelweis. In 1923 he began a series of historical lectures before the medical society, for which he was awarded a prize by the society. In 1928 he was invited by the medicohistorical institute in Leipzig, Germany, to lecture. The Ministry of Public Instruction delegated him to represent the Hungarian university at foreign medical congresses in sixteen instances. In 1930 he was entrusted with writing the history of the faculty of medicine of the Peter Pazmany University, Budapest, on the occasion of its tercentenary. This is his most valuable work.

#### Marriages

PAUL H. RHODES, Albemarle, N. C., to Miss Ruth Draper of Belmont, Mass., August 13.

THOMAS VIRGIL BANKS to Miss Stella Jane Hulen, both of Hughes, Ark., in September.

JOSEPH M. CHISHOLM, Brighton, Tenn., to Miss Frances Scott of Fayetteville, Tenn., September 3.

ROBERT LATEINER, New Rochelle, N. Y., to Miss Dorothy Kasenetz of Mount Vernon, at Bedford Hills, July 6.

CECIL R. GILBERTSEN, Janesville, Wis., to Miss Dorothy Agnes Buell of Watertown, August 6.

LEO R. WEINSHIEL to Miss Ruth Padway, both of Milwaukee, August 18.

MARK TEMKIN, Beaver Dam, Wis., to Miss Pearl Ann Solomon of Racine, August 9.

## Deaths

**William Henry Seemann** \* New Orleans; Medical Department of Tulane University of Louisiana, New Orleans, 1900; member of the House of Delegates of the American Medical Association, 1915-1916, 1919-1926 and 1930-1938; professor of hygiene at his alma mater and formerly professor of hygiene and tropical medicine at the New Orleans Polyclinic; at one time city bacteriologist; member of the American Society of Clinical Pathologists; at the 1938 session of the American Medical Association in San Francisco he accepted the first Distinguished Service Medal of the Association on behalf of Dr. Rudolph Matas, New Orleans, who was chosen to receive the award but was unable to be present at the meeting; aged 60; died, November 19.

**J. Norman Henry** \* Philadelphia; University of Pennsylvania Department of Medicine and Surgery, Philadelphia, 1895; member of the House of Delegates of the American Medical Association from 1926 to 1931 and in 1933; past president of the Medical Society of the State of Pennsylvania and the Philadelphia County Medical Society; director, department of public health, Philadelphia, from 1932 to 1936; formerly clinical professor of medicine, Woman's Medical College of Pennsylvania; served during the World War; consulting physician to the Pennsylvania Hospital; formerly manager of the Christ Church Hospital; at one time trustee of the University of Pennsylvania; aged 65; died, October 4.

**Frank Cary** \* Greenbush, Wis.; Rush Medical College, Chicago, 1882; member of the Illinois State Medical Society; fellow of the American College of Surgeons; served during the World War; at one time lecturer in pathology, professor of pathology and professor of internal medicine at the Woman's Medical College, Chicago; senior obstetrician to St. Luke's, Michael Reese and Lying-In hospitals, Chicago; the pavilion at the Chicago Lying-In Hospital was named in his honor; aged 80; died, September 8, of coronary insufficiency, hypostatic pneumonia and arteriosclerosis.

**John Harper Girvin** \* Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1892; associate professor of gynecology at the Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania; instructor in gynecology at his alma mater, 1894-1900 and demonstrator of obstetrics, 1895-1915; fellow of the American College of Surgeons; secretary of the College of Physicians, 1918-1934; served on the staff of the Presbyterian Hospital in various capacities; aged 69; died, October 23.

**Howard Anderson McCordock**, St. Louis; University of Buffalo School of Medicine, 1923; professor of pathology at the Washington University School of Medicine; formerly assistant pathologist to the Buffalo General Hospital, 1923-1924; national research fellow in medicine, Johns Hopkins University, Baltimore, 1924-1927; member of the American Association of Pathologists and Bacteriologists and the American Society for Experimental Pathology; aged 43; died, November 13, in the Barnes Hospital of aortic stenosis.

**Henry Otto Wyneken** \* San Antonio, Texas; Chicago College of Medicine and Surgery, 1912; past president and secretary of the Bexar County Medical Society; served during the World War; chairman of the board of managers of the Robert B. Green Hospital; physician in charge of the Grace Lutheran Sanatorium, 1913-1915; organizer and first president of the city association for the blind; aged 52; on the staff of the Santa Rosa Hospital, where he died, September 14, of pulmonary embolism.

**Alfred F. Van Horn** \* Plainfield, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1884; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; past president of the Union County Medical Society; for many years school physician; on the staff of the Muhlenberg Hospital; aged 77; died, September 30, of coronary thrombosis.

**Joseph Marvin Ferguson**, South Carrollton, Ky.; Kentucky University Medical Department, Louisville, 1902; member of the American Psychiatric Association; served during the World War; at one time surgeon in the U. S. Public Health Service and on the staffs of various Veterans Administration facilities; formerly county health officer; aged 60; died, September 21.

**James Joseph McGuire** \* Trenton, N. J.; University of Pennsylvania Department of Medicine and Surgery, Philadelphia, 1900; secretary of the state board of medical examiners;

fellow of the American College of Physicians; on the staffs of St. Francis Hospital and the Orthopedic Hospital; aged 62; died, October 11, of arteriosclerosis, uremia and nephritis.

**Gaston Lefebvre de Bellefeuille**, Montreal, Que., Canada; M.B., Laval University Medical Faculty, Montreal, 1903, and M.D. in 1905; Laval University Faculty of Medicine, Quebec, 1906; professor of clinical psychiatry at the University of Montreal Faculty of Medicine; member of the American Psychiatric Association; aged 56; died in September.

**Thomas Buttermore Echard**, St. Petersburg, Fla.; University of Pennsylvania Department of Medicine and Surgery, Philadelphia, 1901; member of the Florida Medical Association; formerly on the staffs of the Mound Park Hospital, St. Anthony's Hospital and the American Legion Crippled Children's Hospital; aged 60; died, September 24.

**Henry Theodor Von Deesten** \* Jersey City, N. J.; Columbia University College of Physicians and Surgeons, New York, 1901; fellow of the American College of Physicians; on the staffs of the Christ Hospital, Jersey City, St. Mary Hospital, Hoboken and Bayonne (N. J.) Hospital; aged 58; died, September 1, of angina pectoris.

**Louis Joseph Bragman** \* Binghamton, N. Y.; Syracuse University College of Medicine, 1921; member of the American Psychiatric Association; for many years affiliated with his alma mater in various teaching capacities; on the staff of the Syracuse Psychopathic Hospital; aged 40; died, October 12, in the City Hospital of pneumonia.

**Henry Alexander Sussman** \* Brooklyn; Columbia University College of Physicians and Surgeons, New York, 1915; formerly assistant clinical professor of medicine, Long Island College of Medicine; served during the World War; on the staff of the Jewish Hospital; aged 47; died, October 16, of heart disease.

**James Ernest Daniel**, Greenville, S. C.; Medical College of the State of South Carolina, Charleston, 1905; member of the South Carolina Medical Association; served during the World War; city physician; formerly associate editor of the *Journal of the South Carolina Medical Association*; aged 55; died, September 24.

**Frank Allen Benedict**, Seymour, Conn.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1887; member of the Connecticut State Medical Society; aged 77; died, September 13, of arteriosclerosis, hypertension, cerebral thrombosis, cardiac infarction and bronchopneumonia.

**Cornelius Joseph McGillicuddy**, Boston; Harvard University Medical School, Boston, 1896; veteran of the Spanish-American and World wars; formerly connected with the U. S. Veterans Bureau; aged 67; died, September 15, in Chelsea of arteriosclerotic heart disease and cirrhosis of the liver.

**Victor Hugo Dye**, Sistersville, W. Va.; Maryland Medical College, Baltimore, 1901; member of the West Virginia State Medical Association; county coroner; aged 61; died, September 27, in the Ohio Valley General Hospital, Wheeling, of perforated gastric ulcer and peritonitis.

**Charles Vilas Martin** \* Maryville, Mo.; Hahnemann Medical College and Hospital, Chicago, 1901; at one time adjunct professor of pediatrics and clinical instructor at his alma mater; on the staff of St. Francis Hospital; aged 59; died, September 25.

**Arthur Lionel Patch** \* Windsor, Vt.; Harvard University Medical School, Boston, 1909; past president and secretary of the Windsor County Medical Society; on the staff of the Windsor Hospital; aged 58; died, September 17, of malignant hypertension.

**John Charles Lynch**, Kansas City, Mo.; Medico-Chirurgical College of Kansas City, Mo., 1905; member of the Missouri State Medical Association; veteran of the Spanish-American and World wars; aged 69; died, September 15, of coronary thrombosis.

**William Wheelock Quinlan** \* Wilmette, Ill.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1891; medical referee of the Mutual Life Insurance Company; aged 71; died, September 24, of heart disease.

**Theodore Williams Ely**, Manchester, Mass.; Western Reserve University Medical Department, Cleveland, 1909; member of the Massachusetts Medical Society; served during the World War; aged 53; died, September 25, of coronary heart disease.

**James Rodolph Taylor** \* Sidney, Neb.; University College of Medicine, Richmond, 1907; past president of the Cheyenne County Medical Society; medical superintendent of the Taylor Hospital; aged 58; died, September 1, of coronary thrombosis.

**Joseph Ezra Wells** ♂ Cynthiana, Ky.; Medical College of Ohio, Cincinnati, 1881; past president of the state board of health and the Kentucky State Medical Association; on the staff of the Harrison Memorial Hospital; aged 77; died, September 3.

**Augustus Edwin Simonton** ♂ Jonesboro, La.; College of Physicians and Surgeons, Baltimore, 1883; for many years bank president; aged 77; died, September 12, in a sanatorium at Dallas, Texas, of cerebral hemorrhage and arteriosclerosis.

**John Luther Nall**, Danville, Va.; North Carolina Medical College, Davidson, 1905; member of the Medical Society of Virginia; aged 61; on the staff of the Memorial Hospital, where he died, September 30, of myelogenous leukemia.

**Arthur Aldridge**, Richmond Heights, Mo.; University of Louisville (Ky.) Medical Department, 1872; aged 88; died, September 24, in Manchester of bronchopneumonia, uremia, chronic myocarditis, arteriosclerosis and nephritis.

**Benjamin Wallace Vitou** ♂ A. Surg., Lieut. (j. g.) U. S. Navy, Portland, Ore.; Creighton University School of Medicine, Omaha, 1936; aged 26; was drowned recently at Chefoo, China, where he was stationed aboard the U. S. S. *Ford*.

**Charles Edmund Stewart**, Palmer, Iowa; College of Physicians and Surgeons, Keokuk, 1887; member of the Iowa State Medical Society; aged 75; died, September 3, in St. Joseph Mercy Hospital, Fort Dodge, of coronary sclerosis.

**Samuel Tilden Silverman**, New York; Columbia University College of Physicians and Surgeons, New York, 1906; aged 54; died, September 8, in the Mount Sinai Hospital of carcinoma of the splenic flexure of the colon.

**James E. Gudge**, Cynthiana, Ind.; Medical College of Evansville, Ind., 1883; member of the Indiana State Medical Association; formerly bank president; aged 80; died, September 12, of heart disease and arteriosclerosis.

**John Francis Morgan**, Joplin, Mo.; Columbus Medical College, 1881; member of the Missouri State Medical Association; aged 83; died, September 2, in St. John's Hospital of cerebral thrombosis and arteriosclerosis.

**Bismarck Ferguson**, Houston, Texas; University of Texas School of Medicine, Galveston, 1903; veteran of the Spanish-American War; aged 61; died, September 22, in the Methodist Hospital of carcinoma of the stomach.

**Samuel Beatty Robb**, Leonard, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1892; aged 69; died, September 26, in the University Hospital, Ann Arbor, of monocytic leukemia.

**Aaron Albert York**, Empire, Ala.; Birmingham Medical College, 1906; member of the Medical Association of the State of Alabama; aged 59; died, September 24, of heart disease, hypertension and arteriosclerosis.

**Vance Lee Fitzgerald** ♂ Barrington, R. I.; Bellevue Hospital Medical College, New York, 1895; fellow of the American College of Surgeons; aged 75; died, September 24, in the Memorial Hospital, Pawtucket.

**William Thaddeus McRea**, North Little Rock, Ark.; University of Arkansas School of Medicine, Little Rock, 1912; aged 57; died, September 13, in the Veterans Administration Facility, North Little Rock.

**Jacob Austin Knight**, Orient, Ohio; Starling Medical College, Columbus, 1903; visiting physician at the Institution for Feeble-minded for many years; aged 66; died, September 23, of pulmonary tuberculosis.

**Carl Neu**, Seattle; Kaiser-Wilhelms-Universität Medizinische Fakultät, Strassburg, Germany, 1901; aged 64; died, September 28, of bronchopneumonia, cerebral hemorrhage and hypertensive heart disease.

**Benjamin Aiken Phillips**, Houston, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1893; veteran of the Spanish-American War; aged 71; died, September 12, of heart disease.

**James Ashley Mourfield**, Lenoir City, Tenn.; Vanderbilt University School of Medicine, Nashville, 1883; member of the Tennessee State Medical Association; aged 83; died, September 16, of heart disease.

**Vernon Tarver** ♂ Star City, Ark.; University of Arkansas School of Medicine, Little Rock, 1926; county coroner; served during the World War; aged 40; died, September 11, in a hospital at Little Rock.

**Otto L. Sahlender**, St. Louis; St. Louis Medical College, 1896; member of the Missouri State Medical Association; aged 68; died, September 8, of carcinoma of the stomach and pulmonary tuberculosis.

**William C. Weber** ♂ Cleveland Heights, Ohio; Starling Medical College, Columbus, 1888; an Affiliate Fellow of the American Medical Association; aged 79; died, September 15, of bronchopneumonia.

**Mary Gould Hood**, Boston; Woman's Medical College of Pennsylvania, Philadelphia, 1874; member of the Massachusetts Medical Society; aged 88; died, September 19, at the Waltham (Mass.) Hospital.

**Hugh McGuire** ♂ Alexandria, Va.; University College of Medicine, Richmond, 1894; on the staff of the Alexandria Hospital; aged 67; died, September 7, of cerebral thrombosis and arteriosclerosis.

**William Holmes Crowley**, Hartford, Conn.; University of Buffalo School of Medicine, 1890; on the staff of St. Francis Hospital; aged 72; died, September 12, of angina pectoris and hypertension.

**James H. Madden**, Colorado Springs, Colo.; Missouri Medical College, St. Louis, 1885; member of the Colorado State Medical Society; aged 78; died, September 26, of coronary thrombosis.

**William Meredith**, Beaverdam, Va.; Medical College of Virginia, Richmond, 1886; for many years member of the county school board; aged 73; died, September 9, of coronary occlusion.

**John Henry Mayer**, Lakeland, Fla.; Baltimore Medical College, 1902; formerly superintendent of the Chambersburg (Pa.) Hospital; aged 60; died, September 10, of cardiac decompensation.

**Wallace E. Steele**, Carthage, Mo.; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1901; aged 84; died suddenly, September 13, of chronic myocarditis and angina pectoris.

**Wendell Tracy Smith**, Pontiac, Mich.; University of Michigan Medical School, Ann Arbor, 1927; for many years county physician; aged 53; died, October 6, in St. Joseph Mercy Hospital.

**William Madison Young**, Jefferson, Iowa; College of Physicians and Surgeons, Keokuk, 1881; member of the Iowa State Medical Society; aged 81; died, September 30, of angina pectoris.

**Harry H. Smith**, Oxford, Ohio; Medical College of Ohio, Cincinnati, 1883; member of the Ohio State Medical Association; aged 76; was killed, September 9, in an automobile accident.

**Philip Carl Matthei**, Chicago; Rush Medical College, Chicago, 1902; aged 57; died, September 2, in the Augustana Hospital of carcinoma of the rectum and mesenteric thrombosis.

**Henry H. Darby**, Omaha; College of Physicians and Surgeons, Keokuk, Iowa, 1883; aged 78; died, September 11, in the Clarkson Hospital of uremia and hypertrophy of the prostate.

**George Arlington Brown**, Winnipeg, Man., Canada; Manitoba Medical College, Winnipeg, 1904; aged 63; died, September 27, in the Deer Lodge Hospital, St. James, of coronary occlusion.

**Ernest Thornton Williams**, Catawissa, Pa.; Jefferson Medical College of Philadelphia, 1905; member of the Medical Society of the State of Pennsylvania; aged 56; died, August 6.

**Jonathan Dawson Waters**, Saluda, S. C.; Medical College of Georgia, Augusta, 1888; member of the South Carolina Medical Association; aged 71; died, September 23, of nephritis.

**John Thomas Anderson**, Chadburn, N. C.; University of Pennsylvania School of Medicine, Philadelphia, 1917; died, September 8, of cerebral hemorrhage and hypertension.

**Samuel Joseph Turcotte**, Willimantic, Conn.; Middlesex College of Medicine and Surgery, Waltham, Mass., 1921; aged 53; died, September 13, in Norwich of arteriosclerosis.

**Robert Caldwell Milburn**, Muncie, Ind.; Barnes Medical College, St. Louis, 1899; aged 78; died, September 14, of bronchopneumonia, arteriosclerosis and myocarditis.

**Clinton Carl Wright** ♂ Detroit; Cleveland Homeopathic Medical College, 1900; on the staff of the Grace Hospital; aged 62; died, September 14, in the Henry Ford Hospital.

**Pasquale Colio**, Red Bank, N. J.; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1902; aged 62; died, September 15, of cardiovascular renal disease.

**Francis Wayland Adams**, Royalston, Mass.; Harvard University Medical School, Boston, 1868; Civil War veteran; aged 98; died, September 24, of chronic myocarditis.

**William King Stillman Jr.**, Atlanta, Ga.; University of Tennessee College of Medicine, Memphis, 1923; aged 40; died, September 2, of acute dilatation of the heart.



**James Augustus Simpson**, Florence, Ala.; Meharry Medical College, Nashville, Tenn., 1914; aged 61; died, September 27, of cerebral hemorrhage and arteriosclerosis.

**John W. Vaughan** \* St. Louis; St. Louis College of Physicians and Surgeons, 1884; aged 81; died, September 11, in the Missouri Baptist Hospital of pneumonia.

**R. P. Bishop**, Channing, Texas (licensed in Texas, under the Act of 1907), formerly county health officer; aged 68; died, September 23, in a hospital at Amarillo.

**William Harvey Wagoner**, Peru, Ind.; Eclectic Medical Institute, Cincinnati, 1903; secretary of the school board; aged 62; died, September 25, of heart disease.

**Otto Jack Knolle** \* Fayetteville, Texas; University of Louisville (Ky.) Medical Department, 1900; aged 60; died, September 1, of chronic myocarditis.

**Hugh Brown Todd**, Houston, Texas; Marion-Sims College of Medicine, St. Louis, 1898; aged 71; died, September 15, in Garden Villa of coronary occlusion.

**Nathaniel D. Morton**, Richmond, Va.; University College of Medicine, Richmond, 1909; aged 58; died, September 10, of myocarditis and arteriosclerosis.

**Allen M. Chilcote**, Fostoria, Ohio; University of Wooster Medical Department, Cleveland, 1875; aged 87; died, September 29, of cerebral hemorrhage.

**Robert D. Guerry**, Savannah, Ga.; Hospital Medical College, Atlanta, 1911; aged 57; died, September 3, in Bluffton, S. C., of acute myocarditis.

**Albert S. Smith**, Philadelphia; Jefferson Medical College of Philadelphia, 1876; aged 84; died, August 20, of chronic myocarditis and nephritis.

**George Edward Osgood** \* St. Petersburg, Fla.; Harvard University Medical School, Boston, 1887; aged 74; died, September 21, of myocarditis.

**Charles John Aaron** \* Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1901; aged 71; died, September 4, of coronary thrombosis.

**Louis Joseph Piuze**, St. Malachie, Que., Canada; Laval University Faculty of Medicine, Quebec, 1911; mayor; aged 53; died in September.

**William R. Wycoff**, Long Beach, Calif.; Kentucky School of Medicine, Louisville, 1882; aged 78; died, August 21, of coronary thrombosis.

**Burgoyne H. Gibson**, Richmond, Ky.; Hospital College of Medicine, Louisville, 1904; aged 67; died, September 15, of cardiorenal disease.

**Richard Lee Smith**, Waco, Texas; University of Tennessee Medical Department, Nashville, 1885; aged 74; died, September 28, of uremia.

**John J. Morrow**, New Orleans; Flint Medical College of New Orleans University, 1908; aged 56; died, August 27, of diabetes mellitus.

**John Hilliard Knight**, Moose Jaw, Sask., Canada; Queen's University Faculty of Medicine, Kingston, Ont., 1880; aged 80; died, August 7.

**William A. Kendall**, Crescent, Okla.; Baltimore University School of Medicine, 1889; aged 79; died, September 19, of myocarditis.

**Hannah Steele Sparrow**, Chicago; Bennett College of Eclectic Medicine and Surgery, Chicago, 1887; aged 84; died, September 30.

**Edwin Jay Clark**, Denver; Hahnemann Medical College and Hospital, Chicago, 1886; aged 76; died, September 17, of gastric ulcers.

**Fred T. Jones**, Little Rock, Ark.; Meharry Medical College, Nashville, Tenn., 1905; aged 61; died, September 10, of septicemia.

**Orrin Feldor Matthews**, Urania, La.; Memphis (Tenn.) Hospital Medical College, 1906; aged 58; died, August 27, of pneumonia.

**Robert J. Gardiner**, Biggar, Sask., Canada; McGill University Faculty of Medicine, Montreal, Que., 1902; died, August 8.

**Fred Siddens**, Bowling Green, Ky.; Barnes Medical College, St. Louis, 1902; aged 57; died, September 9, of cerebral hemorrhage.

**Louis Grear**, Cincinnati; Medical College of Ohio, Cincinnati, 1895; aged 66; died, September 2, in Loveland, Ohio.

**Harry Herbert Alger**, Stirling, Ont., Canada; Trinity Medical College, Toronto, 1893; aged 71; died, September 4.

## Correspondence

### NO AMINOPYRINE IN "ANALGIA" AND "ANTABS"

*To the Editor:*—In Dr. Kracke's paper on the relation of drug therapy to neutropenic states in THE JOURNAL, October 1, he includes on page 1259 a list of preparations described as containing aminopyrine. In this list appear the names of two of our products, namely "Analgia" and "Antabs," neither of which contains aminopyrine. The product marketed under the name "Antabs" is a comparatively simple antacid tablet containing calcium and magnesium carbonates and bismuth subnitrate; the other product, "Analgia," contains acetylsalicylic acid, acetophenetidin and caffeine.

THE WILLIAM S. MERRELL COMPANY,  
E. G. GERWE, Cincinnati.

Director of Laboratories.

### ASCORBIC ACID CONTENT OF COMMERCIAL CANNED TOMATOES AND TOMATO JUICE

*To the Editor:*—A report of the Council on Foods appearing on page 650 of the February 26 issue of THE JOURNAL included a tabulation of the vitamin C content of various canned fruit juices and of sixteen brands of commercially canned tomato juice. Work done here during the past year supplements this report and also points out the variation which may be expected in different brands of commercially canned tomatoes and tomato juice and in different samples of the same brand.

TABLE 1.—Ascorbic Acid Content of Commercially Canned Tomato Juice

Brand	No. of Cans Tested*	Milligrams of Ascorbic Acid per Cubic Centimeter			
		Maximum	Minimum	Average	Standard Deviation
A	12	0.20	0.15	0.17	± 0.021
B	12	0.17	0.15	0.16	± 0.007
C	12	0.19	0.12	0.15	± 0.021
D	12	0.26	0.20	0.23	± 0.015
E	12	0.22	0.08	0.15	± 0.041
F	12	0.19	0.12	0.14	± 0.019
G	12	0.15	0.09	0.14	± 0.017
H	12	0.20	0.14	0.18	± 0.021
I	12	0.22	0.16	0.18	± 0.019
J	12	0.23	0.11	0.18	± 0.034
K	12	0.24	0.11	0.16	± 0.027

\* The contents of each can were thoroughly mixed; triplicate samples were then analyzed for ascorbic acid.

TABLE 2.—Ascorbic Acid Content of Commercially Canned Tomatoes

Brand	No. of Cans Tested*	Milligrams of Ascorbic Acid per Cubic Centimeter			
		Maximum	Minimum	Average	Standard Deviation
E	10	0.21	0.13	0.17	± 0.020
L	10	0.22	0.13	0.19	± 0.026
D	10	0.21	0.16	0.19	± 0.013
M	10	0.21	0.15	0.18	± 0.021
K	10	0.20	0.14	0.18	± 0.015
J	10	0.22	0.15	0.18	± 0.020

\* The contents of an entire can were sieved, and triplicate samples of the resultant mixture were analyzed for ascorbic acid.

The cans were purchased from retail stores in Washington, D. C., at approximately two week intervals between April and November 1937, so that tomatoes canned during the summers of 1936 and 1937 are presumably represented. All determinations of ascorbic acid were made by the indophenol titration technic of Musulin and King (*J. Biol. Chem.* **116**:409 [Nov.] 1936). The values are given in the accompanying tables. The study shows that the variation in ascorbic acid content from can to can of a single brand may be greater than the varia-

tion from brand to brand. Probably both the variety and the condition of the tomatoes contributed to these differences. A study from this laboratory on home-canned tomatoes showed that fresh tomatoes of a single variety from the same plot of ground varied from 0.11 to 0.23 mg. of ascorbic acid per cubic centimeter, depending on the condition of the tomatoes. MacLinn, Fellers and Buck (*Am. J. Hort. Sc.* 34:543, 1937) have shown that different varieties of tomatoes vary from 0.09 to 0.59 mg. of ascorbic acid per gram. In the present study the higher values of some brands, in particular brand D tomato juice, probably indicate the use of good quality tomatoes of a variety high in vitamin content.

OLIVE E. McELROY, PH.D.

HAZEL E. MUNSELL, PH.D.

Washington, D. C.

Bureau of Home Economics,  
U. S. Department of Agriculture.

### AMERICAN HISTORY AS TOLD BY POSTAGE STAMPS

*To the Editor:*—In the correspondence column of THE JOURNAL, September 3, is a note from Dr. Evon Walker of Ottumwa, Iowa. He cites my booklet "American History as Told by Postage Stamps" as the source of information to the effect that a doctor has appeared on an American postage stamp. Your editorial note following Dr. Walker's letter expands a bit on the life of the man in question, Manasseh Cutler. Other letters of inquiry have come, asking for more information about the medical accomplishments of the only physician to be so honored in our history. Further search of material has revealed the following information relative to his medical training (from Parker, William, and Cutler, Julia Perkins: *Life, Journals and Correspondence of Rev. Manasseh Cutler, Cincinnati, Robert Clarke & Co., 1888*):

Soon after his return from the Rhode Island expedition (September 1778), Mr. Cutler decided upon qualifying himself to practice medicine, with a view, probably, to increase his means of usefulness, and also to secure an increase of income adequate to the wants of a growing family. He provided himself with the works of a number of valuable medical authors, and commenced his studies under the direction of his friend and parishioner, Dr. Elisha Whitney. He likewise accompanied the Doctor in his daily visits to his patients, in order to study symptoms and development of disease. With a mind well disciplined to study, his progress was rapid. He comprehended almost at a glance the leading principles of the science, and in a very short period won for himself among the medical profession the reputation of a safe and skilful practitioner. . . .

On June 13, 1785, Mr. Cutler addressed the following letter to Dr. N. W. Appleton: Sir: I have received your letter inclosing an extract from the Records of the Massachusetts Medical Society, by which I am informed that the Society has been pleased to elect me an honorary Fellow. I very sensibly feel the honor conferred upon me by so learned and respectable a Society. This mark of attention is the more flattering as the Medical Art is not my profession. Please to express my acceptance and my warmest acknowledgments to the Society for the honor they have done me. . . .

This doctor-merchant-lawyer-preacher-statesman is shown on the 3 cent stamp commemorating the one hundred and fiftieth anniversary of the Northwest Territory, by reason of his organizing the project. The Northwest Territory was created by the ordinance of 1787, which made the land bounded by the Ohio and Mississippi rivers, the Great Lakes and New York an integral portion of the United States. Colonization was hastened and provisions were made for self government in the new land. So far as I have been able to determine, no other person whose face appears on a stamp of the United States was a qualified member of the medical profession.

CHARLES C. GILL, M.D., Denver.

Fitzsimons General Hospital.

## Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

### MULTIPLE BLOOD TRANSFUSIONS

*To the Editor:*—I should like to know whether there is any danger associated with giving too many transfusions over a period of a month. I had planned on giving three a week for two weeks or longer, but it seems to me that I have read somewhere that too many transfusions may do more harm than good.

M.D., North Carolina.

ANSWER.—The unquestionably great benefits of multiple blood transfusions are occasionally offset by serious or fatal accidents. These can usually be traced to technical errors. Mistakes in grouping or in labeling donors have been responsible for the majority of these tragedies, although some have resulted from other errors in technic. It is well known that a suitable donor's blood may not be compatible with the same recipient ten days later, and severe anaphylactic reactions may occur, probably as the result of iso-agglutinins or of the development of intragroup type (Culbertson, C. G., and Ratcliffe, A. W.: *Reaction Following an Intragroup Blood Transfusion, Am. J. M. Sc.* 192:471 [Oct.] 1936). When a patient requires repeated transfusions, careful cross typing must be done immediately preceding each transfusion. In spite of such care, it has been maintained by many observers that reactions are more frequent after a number of transfusions have been given. Frequently the benefits seem less after a series of transfusions, but there are so many conditioning factors to be considered, such as the progress of the underlying disease and lack of further response of the bone marrow, that this impression must be guarded. On the other hand, Clute (Hemorrhage in Obstructive Jaundice: Case Report with Recovery After Twelve Transfusions, *S. Clin. North America* 13:609-615 [June] 1933) reported a case in which twelve transfusions were given within a week and the patient's life was undoubtedly saved thereby. When large quantities are deemed necessary, Marriott and Kekwick (Continuous Drip Blood Transfusion, *Proc. Roy. Soc. Med.* 29:337-338 [Feb.] 1936) advise the use of the drip method with oxygenation of citrated blood. They have given as much as 5,620 cc. in fifty-one and a half hours, raising the content of hemoglobin from 20 to 88 per cent without untoward results. There are many cases on record in which a greater number of transfusions has been used than that contemplated by the inquirer. The benefits vary with the indications for the transfusions and the curability of the underlying disease.

### "CHROME HOLES"

*To the Editor:*—I have an industrial accident problem at one of our local factories where a good deal of chromium plating is done. The chromium bath is a solution of chromic acid. Whenever the operative has a slight defect in the skin, such as a small scratch, the acid or the acid fumes working into the skin produce an indolent ulcer. These ulcers do not heal if the operative continues at work, even if the hands are protected by rubber gloves, as the acid or the fumes seem to get in in some way. The ulcerative lesions on the hands and fingers will heal fairly well whenever the operative is taken away from this type of work, but it is difficult to do this always. Can you suggest any sort of a protective or medicated dressing which will permit healing of these small skin areas and still allow the operative to continue his work?

C. R. ABBOTT, M.D., Clinton, Mass.

ANSWER.—Unlike ordinary acids, chromic acid is not readily hydrolyzed by those chemicals making up flesh. As a result, the action of chromic acid persists indefinitely, leading to deep "chrome holes."

If the lesion or lesions are small and superficial, it may prove desirable to scrub off the damaged tissues thoroughly with 5 per cent sodium hyposulfite solution or even with water or saline solutions. The purpose of this treatment is to dislodge and remove all tissue containing chromium compounds so that additional damage may not be done by burrowing. After this scrubbing, the wound may be treated just as is any abrasion of similar severity.

If the damage already done is extensive and the chrome holes are too deep for this action, wet dressings of sodium hyposulfite should be applied for a period of from three to five days. This will result in some hastening of the reduction of the chromium compound but apparently does not lead to the dislodgment of the chromium in the flesh. Then wet dressings of

a 5 to 10 per cent solution of sodium citrate, sodium lactate or potassium and sodium tartrate should be applied for the purpose of stripping the chromium from the tissues. Such dressings may be continued for another period of three to five days, depending on the severity of the condition. After that time the treatment ordinarily may take on the character appropriate for any ulcer. Not infrequently it becomes necessary to remove the necrosed tissue in the ulcer by curettage, since this affected flesh acts as a foreign body.

In some instances the treatment may be carried out during the continuation of work, but additional exposure is undesirable and it is often preferable to remove the worker from his customary duties, at least during the early stages of treatment.

#### INTRACTABLE VESICULAR DERMATITIS

*To the Editor:*—A white woman aged 30, not employed, has minute vesicles, which first appear intracutaneously and contain a thin colorless fluid. The vesicles rupture and there is a denuded area underneath which continues to exude a colorless fluid with no crust formation. The lesions are intensely pruritic. Since the vesicles are about 2 mm. apart, there is a confluence of the denuded area. The lesions first appeared on the dorsum of both great toes in a symmetrical arrangement; they next appeared on the dorsum of the feet and tibial surface of the legs about the middle third. The next involvement was the medial side of the hands just medial to the hypothenar eminences. The involvement of the hands has included the dorsum of the first two digits of both hands. The lesions have developed over a period of eighteen months. Smears reveal no bacteria nor fungi, although intradermal tests show the patient sensitive to fungus. The patient is generally in good health, well nourished and with no gynecologic lesions. She is subject to hay fever, being sensitive to ragweed; there have been extensive attempts to desensitize her without success. Dermatologic treatment during the last year has been extensive and varied but unsuccessful. It has consisted of successive uses of salicylic acid 5 per cent in glycerin; Whitfield's ointment, one-half strength; superficial x-rays in sufficient amount; fungus extract given subcutaneously in desensitizing doses, accompanied by phenobarbital one-half grain (0.03 Gm.) twice a day; ultraviolet therapy; ammoniated mercury ointment (U. S. P. strength); oxyquinoline sulfate, 0.4 Gm., triethanolamine, 3 Gm., crude coal tar ointment; Novoxil (Squibb), a colloidal silver preparation, and resorcinol, 1 Gm. Prescriptions containing oxyquinoline have given the most benefit and were combined with sun baths to the affected areas. At present the lesions are unchecked and affect the dorsum of one foot and both hands. New vesicles are appearing on the extensor surfaces of both hands. I am unable to find systemic or nervous disorders which might be a cause and am at the end of my remedies. Can you suggest tentative diagnosis and treatment?

M.D., Ohio.

*ANSWER:*—Judging from the positive response to the intradermal test, the patient has at some time had an infection with ringworm fungus. This often results in sensitization, which is particularly likely to occur in a person with other forms of sensitization such as hers to ragweed. It is often difficult, sometimes impossible, to determine the cause of a dermatitis, though the cause of the accompanying hay fever may be easily discovered. It would be of interest to know whether her dermatitis is worse during the ragweed season.

The first principle of treatment for an acute or subacute dermatitis is to soothe it. In weeping conditions one should apply soothing and astringent wet dressings, such as solution of aluminum subacetate diluted with about sixteen parts of cool water and applied as a thin wet dressing, not covered, but free evaporation being allowed. When the dressing becomes warm, it should be wrung out of the cool solution and reapplied. This should be kept up for a half hour to an hour, then the skin dabbed dry and calamine lotion or a dusting powder applied, either of which may contain 0.5 per cent phenol and 0.25 per cent menthol. The wet dressings should be reapplied every few hours.

After this treatment has stopped the oozing, zinc paste may be used, spread thinly. One per cent phenol may be used in it. If thought necessary to remove it, oil should be used, with great care to avoid rubbing, which may start the itching again. All forms of irritation, dust, soap and water and especially rubbing and scratching, must be avoided. As improvement from this application ceases, one may use stimulation, testing it out on a small area before applying it to the whole surface. Crude coal tar or oil of cade may be added to the zinc paste in small percentage which may be increased as the improvement again stops. When an exacerbation occurs, as it no doubt will, treatment must be started at the beginning and followed out as before. If aluminum acetate is not well borne, a saturated solution of boric acid may be used instead.

Ultraviolet radiation in suberythema doses may be helpful. If roentgen rays are used again to obtain temporary relief, the special susceptibility of the blood vessels in the extremities to this agent must be kept in mind and no stimulating local application used at the same time.

Rest should be ordered and sedatives used, if necessary, to obtain it. Sedatives often seem to have a directly beneficial effect on the dermatitis; but this may be secondary to general lessening of nervous tension and of scratching. General ultraviolet exposures or intramuscular injections of the patient's own blood may have a favorable alternative effect.

#### IRON METABOLISM

*To the Editor:*—Have any experimental data been published showing the disposition of the total amount of ferrous sulfate and iron ammonium citrate ingested daily, as follows: 1. The percentage of iron required to raise the hemoglobin 1 per cent a day where the animal has a secondary anemia with a hemoglobin of less than 50 per cent? 2. The percentage of iron stored in the iron depots of the body? 3. The percentage of iron eliminated? I would appreciate references.

M.D., New York.

*ANSWER:*—It is impossible to give a short and specific answer to this question, since there are a number of variable factors involved which have not been stated.

In man the amount of ferrous sulfate or iron ammonium citrate required daily to raise the hemoglobin 1 per cent a day when the hemoglobin is under 50 per cent is not constant. That is, in some cases 0.4 Gm. (6 grains) of ferrous sulfate is sufficient; in others, two or four times as much may be required. This variation is presumably due to variations in absorption and possibly in utilization and excretion; 0.8 Gm. (12 grains) of ferrous sulfate daily or 6 Gm. (90 grains) of iron ammonium citrate daily is sufficient to give this response in the majority of instances.

The percentage of iron stored in the iron depots of the body in anemic patients is not definitely known. In a few experiments in which iron has been given parenterally, there has been a quantitative utilization of the iron to form hemoglobin. Thus it would appear that in this case little or no iron was stored.

Only a relatively small amount of the iron ingested is actually absorbed. Hence the amount of iron eliminated will vary with the iron taken into the body.

#### References:

- Hahn, P. F.: The Metabolism of Iron, *Medicine* 16:249 (Sept.) 1937.  
Heath, C. W., and Patek, A. J., Jr.: The Anemia of Iron Deficiency, *Medicine* 16:267 (Sept.) 1937.  
Fullerton, H. W.: The Treatment of Hypochromic Anemia with Soluble Ferrous Salts, *Edinburgh M. J.* 41:99 (Feb.) 1934.

#### TRAUMATIC SYNOVITIS

*To the Editor:*—A man received a blow on the right knee from a wheel barrow while at work. The accident was not reported. Three weeks later he had a swollen right knee joint which made walking difficult. Physical examination indicated fluid in the joint and also in the prepatellar bursa. I aspirated and found the fluid to be bloody, of a dark color, and the fluid portion fairly clear; that is, it was not xanthochromic, as one might expect if the blood had been there three weeks. I banded the knee and ordered rest. The patient returned three days later with the hydrops recurrent; aspiration showed bloody fluid as found before but not so concentrated. A week later he returned and was put to bed in the hospital for a week, the fluid disappearing almost entirely. He was discharged and was no longer under my care. Now he is suing for compensation and I must give my opinion. Was the injury of three weeks' duration when I saw him first? Is there any way of answering the question from the nature of the fluid I aspirated? On taking a roentgenogram of the joint I saw several round opaque bodies near the joint surface posteriorly. He gave no history of locking symptoms at any time or of any disability of the joint. When I had emptied the patella bursa I could palpate movable bodies in or about this bursa. They did not show on the roentgenogram. I should appreciate any reference to authorities.

M.D., Wyoming.

*ANSWER:*—The nature of the fluid can be explained on the basis of a hemorrhage with a superimposed traumatic synovitis. The hemorrhage evidently stopped and the synovitis continued.

In regard to the direct question, Was the injury of three weeks' duration when the physician first saw the patient, the answer is yes.

The foreign bodies or joint mice are due to osteochondritis dissecans. If these bodies are not caught between the joint surfaces there is no locking. They may be found in any portion of the joint and in the quadriceps bursa.

The knee should be studied in three roentgen projections. If it is possible to bend the knee to 135 degrees, the central ray should be directed from behind; i. e., the so-called Holmblad-Béclère projection.

#### References:

- Brahdry, Leopold, and Kahn, Samuel, editors: *Trauma and Disease*, Philadelphia, Lea & Febiger, 1937.  
McBride, E. D.: *Disability Evaluation*, Philadelphia, J. B. Lippincott Company, 1937.  
Fisher, A. G. T.: *Internal Derangements of the Knee Joint*, New York, Macmillan Company, 1933.

**ETHYL CHLORIDE AND NITROUS OXIDE**

To the Editor:—Please let me know regarding the relative safety of the primary induction of anesthesia in children by ethyl chloride and gas-oxygen. I have seen the former used a good deal lately and have not been favorably impressed with the patient's reaction to it, there being some cyanosis and the blood being darker than normal. However, the anesthetist tells me that where she was trained it is used in a routine manner as a primary anesthetic for children. I have understood that gas-oxygen was not used in children under 8 or 10 years of age for induction purposes. Am I correct in this assumption?

M.D., Massachusetts.

ANSWER.—Ordinarily it is considered safer to use nitrous oxide and oxygen than to use ethyl chloride for induction of anesthesia, although ethyl chloride has been used numerous times in a dental clinic in Boston. Nitrous oxide and oxygen is frequently used for induction of anesthesia in children less than 8 years of age.

**UNUNITED FRACTURES OF RADIUS AND SYRINGOMYELIA**

To the Editor:—A man aged 49, with good nutrition and circulation, presents a fracture of the midradius, ununited after five months. The complicating factor is a nervous lesion of the cord which my associates and I have taken to be a syringomyelia of Morvan's type, producing complete anesthesia of the fractured arm. Tactile sensation is lost as well as pain and temperature distinction. Although this condition is not equal bilaterally, we believe it to be more than an injury to the brachial plexus, and it is, of course, wholly unrelated to the present fracture, preceding it by at least ten years. Should surgery be resorted to? Could healing be expected following open reduction and possible bone graft?

M.D., Ontario.

ANSWER.—The probabilities are that healing of the wound would follow after reduction and the application of the bone graft. Whether the bone graft would bring about union is more doubtful. Certainly the chances would not be as favorable as in a normal arm. Whether to operate or not would depend on the use that the patient had of the arm prior to the accident. If it was of decided value in his work, it might be worth an attempt to secure union. If it was of no use, the operation would not be indicated.

**MEDIUM FOR STREPTOCOCCUS CULTURE**

To the Editor:—Can you tell me which medium would be the best to use in my office for the growth of streptococcus in the throat? I make a routine culture in all cases of acute inflammation and practically never get streptococci. I have been using Loeffler's blood serum-Difco.

M.D., Connecticut.

ANSWER.—Loeffler's blood serum is not a suitable medium for culture of streptococci from the throat. Ordinary Petri plates made with blood agar are best suited for routine culture of material from the throat for streptococci.

**APPENDECTOMY AFTER APPENDICAL ABSCESS**

To the Editor:—In what percentage of cases of appendical abscess treated by drainage only is a secondary operation for removal of the appendix necessary?

M.D., New York.

ANSWER.—The appendix should always be removed at a secondary operation. The date of the secondary operation requires some judgment. From six weeks to six months may be necessary, depending on the patient's condition.

**FIRE EXTINGUISHERS**

To the Editor:—On page 469 in the July 30, 1938, issue of THE JOURNAL you replied to a question on fire extinguishers for x-ray departments. While mention was made of carbon dioxide extinguishers, it was not clear whether or not you meant the liquid carbon dioxide type, which during use evolves a stream of carbon dioxide gas containing a cloud of particles of solid carbon dioxide without any moisture. This type of extinguisher is perfectly safe for use on electrical equipment, since it involves no water or acids. It is also perfectly safe to the user because carbon dioxide is the only gas liberated. It is supplied by Walter Kidde and Company of Bloomfield, N. J.

GEORGE H. SCHNELLER, Corona, N. Y.

**HYSTERECTOMY AND INCIDENCE OF CANCER**

To the Editor:—In THE JOURNAL, Oct. 15, 1938, page 1492, under the Query and Minor Notes heading "Hysterectomy and Incidence of Cancer," appears a quotation from von Graff as follows: "Comparing the 0.6 per cent possibility of cancer after subtotal hysterectomy with the actual frequency of 4 per cent of stump cancer, every unprejudiced observer must admit that the danger of cancerous degeneration, present at the time of operation or developed later, is more than six and a half times as great as ordinarily reckoned." The statistics given do not seem convincing, and there is no proof that there is any definite relationship between the two groups, since neither the normal incidence of cancer is given nor the percentage of operations in an average group.

HENRY G. HADLEY, M.D., Washington, D. C.

# Medical Examinations and Licensure

## COMING EXAMINATIONS

### STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, November 26, page 2036.

**NATIONAL BOARD OF MEDICAL EXAMINERS**

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Medical centers having five or more candidates desiring to take the examination, Feb. 13-15. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th Street, Philadelphia.

**SPECIAL BOARDS**

AMERICAN BOARD OF ANESTHESIOLOGY: An Affiliate of the American Board of Surgery. Written examination, Part I, will be held in various cities of the United States and Canada, April 8. Oral examinations for all candidates, St. Louis, May 13-14. Applications must be filed not later than sixty days prior to the date of the examinations. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF INTERNAL MEDICINE: Written examinations will be held in various parts of the United States, Feb. 20. Application must be received on or before Jan. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Written examination and review of case histories of Group B applicants will be held in various cities of the United States and Canada, Feb. 4. General oral, clinical and pathological examinations for all candidates (Groups A and B) will be given in St. Louis, May 15-16. Applications must be filed not later than sixty days prior to date of examination. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh. (6).

AMERICAN BOARD OF OPHTHALMOLOGY: St. Louis, May 15. Applications must be filed before February 15. Sec., Dr. John Green, 3720 Washington Blvd., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Memphis, Tenn., Jan. 13-14. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: St. Louis, May 12-13. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PEDIATRICS: New York, April 26. Appointments must be made before Dec. 26. St. Louis, May 16. Appointments must be made before Jan. 16. Cincinnati, Nov. 14-15. Appointments must be made before July 14. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 28-30. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: St. Louis, May 11-14. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: New York, Jan. 13-15. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

**Georgia June Examination**

Mr. R. C. Coleman, joint secretary, State Examining Boards, reports the written examination held by the State Board of Medical Examiners at Atlanta and Augusta, June 14-15, 1938. The examination covered ten subjects and included 100 questions. An average of 80 per cent was required to pass. Sixty-seven candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Emory University School of Medicine.....(1937)	83.1, 83.8, 86.7, 86.8, 87.1, 87.2, 87.2, 87.4, 87.6, 87.7, 87.7, 87.8, 88.2, 88.2, 88.4, 88.5, 88.7, 88.9, 89.2, 89.5, 89.7, 89.8, 90.1, 91.2, 91.4, 91.4, 92.4	(1937)	82.8,
University of Georgia School of Medicine.....(1938)	82.5, 83.3, 83.9, 84.6, 84.6, 85, 85.1, 85.3, 85.5, 85.7, 85.7, 85.8, 85.9, 86, 86.4, 86.5, 86.5, 86.7, 86.8, 86.8, 86.9, 87.1, 87.8, 87.8, 88.1, 88.2, 88.6, 88.9, 89, 89.2, 89.8	(1938)	81.8,
School of Medicine of the Division of Biological Sciences (1937)		(1937)	85.7
Tulane University of Louisiana School of Medicine....(1938)		(1938)	86.1
Jefferson Medical College of Philadelphia.....(1937)		(1937)	90.7
Vanderbilt University School of Medicine.....(1937)		(1937)	88, 91.7
University of Texas School of Medicine.....(1937)		(1937)	94.1

Seventeen physicians were licensed by reciprocity and three physicians were licensed by endorsement from June 16 through October 12. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Arkansas School of Medicine.....(1937) Tennessee		(1934)	Arkansas,
Emory University School of Medicine.....(1935)		(1935)	Mississippi
Northwestern University Medical School.....(1936)		(1936)	Oklahoma
Tulane University of Louisiana School of Medicine....(1935)		(1935)	Louisiana
Johns Hopkins University School of Medicine.....(1937)		(1937)	Maryland
Maryland Medical College.....(1906)		(1906)	S. Carolina
St. Louis University School of Medicine.....(1935)		(1935)	Missouri
Univ. of the City of New York Medical Department.....(1891)		(1891)	Virginia
Jefferson Medical College of Philadelphia.....(1932)		(1932)	New Jersey,
Medical College of the State of South Carolina.....(1933)		(1933)	S. Carolina
University of Tennessee College of Medicine.....(1936)		(1936)	Tennessee
Vanderbilt University School of Medicine.....(1898)		(1898)	Tennessee,
(1935) N. Carolina			
Baylor University College of Medicine.....(1928)		(1928)	Texas
University of Texas School of Medicine.....(1937)		(1937)	Texas

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists.....(1937)		(1937)	N. B. M. Ex.
Harvard University Medical School.....(1935)		(1935)	N. B. M. Ex.
Medical College of the State of South Carolina.....(1936)		(1936)	N. B. M. Ex.

## Book Notices

**The Principles and Practice of Medicine: Designed for the Use of Practitioners and Students of Medicine.** By The Late Sir William Osler, Bart., M.D., F.R.C.P. Revised by Henry A. Christian, M.D., LL.D., S.D., Hersey Professor of the Theory and Practice of Physic, Harvard University. The 9th, 10th, 11th and 12th editions of this book were revised by Thomas McCrae. Thirteenth edition. Cloth. Price, \$9. Pp. 1424, with illustrations. New York & London: D. Appleton-Century Company, Incorporated, 1938.

The most famous of all practices of medicine is now in its thirteenth edition and under a new editorship. Previous editions appeared under the editorship of Dr. Thomas McCrae. The following note from the preface by Dr. Henry A. Christian indicates the nature of the changes that have been made:

In the First Edition Osler put much that was based upon his personal experience at bedside or at the autopsy table. In this edition I assume responsibility for all changes and additions, not credited by name to some other; what appears not so credited is based upon my own clinical and pathological experience, much of it acquired at the Peter Bent Brigham Hospital in Boston. In preparing this revision, wisely or unwisely, I have had the assistance or criticism of no one.

The book is now rearranged so that it begins with a general discussion of infections, including the pneumonias, and thereafter takes up other infections in order. Typhoid fever occupies far less space than was required when the book was first published and when typhoid was perhaps the most prevalent of all diseases affecting mankind.

It is, of course, impossible to review even a work as important as this one line by line. The task of keeping a work of such great scope abreast of the times is a difficult one. For instance, most of the data under etiology, history and incidence refer to statistics dating back to 1900 or 1903. While such statistics are historically important, they mean little to the student of 1938. In the discussion of measles there is mention of the use of convalescent serum, but nothing is said of the more recent work with material prepared from the placenta. The section on yellow fever still says that the epidemics in the United States have been in the summer and autumn months, disappearing rapidly with cold weather. This is the same statement that has appeared in earlier editions, yet the last epidemic of yellow fever appeared in the United States in Laredo in 1903. Neither is there mention of the fact that yellow fever may again threaten because of the new discoveries that have been made relative to the residual infection now being found in jungle monkeys.

Most remarkable is the statement on the prophylaxis of syphilis and on its control. This also appeared in earlier editions but is certainly not a reflection of the great activities in relationship to syphilis which prevail today. In the section on amebiasis, reference to the outbreak in Chicago in 1933 says it resulted from sewage, yet this hardly gives a picture of what actually occurred.

The book reflects repeatedly the difficulty of a complete revision of a volume of this character. Today medicine moves so rapidly that only the most serious and consistent effort can maintain the literary virtues of a great volume of this type and, at the same time, provide for that modernity of information which is necessary in any science.

**The Fight for Life.** By Paul de Kruif. Cloth. Price, \$3. Pp. 342. New York: Harcourt, Brace & Company, 1938.

Out of his numerous contributions to the *Country Gentleman*, the *Ladies Home Journal* and the newspapers, de Kruif has assembled these sketches. The series of volumes which have brought his name before the American people as the interpreter of science for the average man now includes "Microbe Hunters," "Hunger Fighters," "Seven Iron Men," "Men Against Death" and "Why Keep Them Alive?"

The present volume is largely concerned with maternal and infant welfare, the heat treatment for disease, infantile paralysis, tuberculosis and syphilis. De Kruif still writes with the fire that characterized his first book. He must, by this time, have seen the impossibility of fulfillment of many of the promises he made in his earlier articles. Once he seemed to think that with artificial pneumothorax tuberculosis could be overcome. More recently he seemed quite convinced that nasal spraying would

prevent the transmission of infantile paralysis on a large scale. He has accepted apparently in toto the concept that maternity hospitals devoted exclusively to mothers in pregnancy would answer the problem of maternal mortality. And he, like many others, seems to feel that with money it is possible to accomplish anything. Actually, of course, it is not possible. Once scientific research has established positively the cause, the method of transmission and the specific method of preventing the disease, it becomes easy to secure money to put into effect the methods that have been established, but even then apparently it is not possible to eliminate the disease entirely.

Yellow fever, once under better control than now, threatens to emerge from the jungle. New diseases, like encephalitis apparently associated with similar conditions in horses, threaten us from time to time. Even with all that we know about diphtheria, there were only a few cities in the United States which were last year without deaths from diphtheria. Money is a help, but knowledge is more important.

De Kruif favors a revolution in our social order. He thinks always of the end and does not disturb himself over the means. Certainly he is a ferment; with a little more restraint and judgment he might have been a high explosive.

**Chronic Rheumatic Diseases: Being the Fourth Annual Report of the British Committee on Chronic Rheumatic Diseases Appointed by the Royal College of Physicians.** Edited by C. W. Buckley, M.D., F.R.C.P. Number Four. Cloth. Price, \$3.25. Pp. 160, with illustrations. New York: Macmillan Company, 1938.

This is announced as the fourth and final volume of the reports issued by the British Committee on Chronic Rheumatic Disease. Arrangements, however, are being made for a new series to appear at more frequent intervals under slightly different auspices. It contains a group of papers of original and distinctive nature. The first, contributed by Davidson and Duthie, is entitled "Can the Voluntary Hospital System Solve the Problem of Rheumatic Disease?" They review some of the economic and social aspects presented by rheumatic disease in Britain and conclude that increased facilities for the care of such patients are badly needed. The volume contains a symposium of three brief papers on sciatica, a paper on rheumatic disease in the horse, and reviews of the present status of the virus problem in acute rheumatism, vaccine therapy in rheumatism, and the use of gold salts in rheumatoid arthritis. The second of the papers on gold therapy, written by Ellman and Lawrence, constitutes a rather favorable report on the results from the use of gold in selected cases of rheumatoid arthritis. Hence, as the only American contributor, has written an excellent paper on the problem of arthritis and rheumatism in the United States. This is one of the most useful of the recent books devoted to rheumatic diseases.

**Embryonic Development and Induction.** By Hans Spemann. Mrs. Hepsa Ely Stillman Memorial Lectures, Yale University. Cloth. Price, \$3. Pp. 401, with 192 illustrations. New Haven: Yale University Press; London: Oxford University Press, 1938.

The processes of early development seem especially baffling when one begins to analyze them as Professor Spemann has done. What is it that guides the orderly sequence of events with the ever increasing complexity of structure and relationship? Some have given up in despair and called in a metaphysical "entelechy" to preside over normal development and to rearrange matters as best it may when something goes wrong. Others, like Spemann, have devoted themselves to uncovering factors concerned in the process. He has not solved the riddle but he is able to report some progress and to point out flaws in theories that have been proposed. He describes many remarkable experiments, analyzing and collating them, evaluating a large body of literature. Any one with biologic interests can follow the argument, although the details will be appreciated only by the embryologists.

The development of newts and salamanders displays vertebrate embryology in diagrammatic form, and the eggs and embryos are unique in that they can be dissected and spliced together without seriously interfering with further development. Just as the adult newt can regenerate a lost limb or optic lens, so certain differentiated parts of an embryo can, when isolated, revert to an undifferentiated condition, reveal remarkable potencies and develop in an apparently purposeful manner. Since grafts can be made from one species to another it is

possible to follow the individual cells of the transplant as they differentiate because of characteristic pigments or cell sizes. A spectacular experiment of Schotte and Spemann's is the transplantation of a bit of ectoderm from a toad embryo to the head region of a newt embryo. Although this transplant would normally have become epidermis, in its new location it produces mouth "furnishings." They are however the characteristic horny plates of the herbivorous toad tadpole, not the teeth of the carnivorous newt larva. Such activation of latent capacities which would never have been expressed normally was termed "induction" by Spemann. It has long been known (Warren Lewis) that the prospective retina (optic vesicle) when transplanted may stimulate the development of a typical lens from the prospective skin. These are cases of specific effect. In other cases the stimulus of induction appears to be no more specific than a localized increase in metabolic rate. In these cases the structure produced depends on the innate capacities of the stimulated cells and the region of the body to which it is grafted. Certain parts of young embryos (prospective notochord cells *par excellence*) may induce a complete accessory embryo, built up in part of transformed host cells, in part of transplant cells. This harmonious union of cells from widely separated species often in a single organ and the orderly arrangement of organs involve an integration which corresponds to the "wholeness" of the normal embryo. Its bearing on the origin of double monsters and teratomas is obvious but is not discussed. Spemann suggests that this "wholeness" is comparable to the psychic integration which underlies our own individuality. This assumes a mechanism of heredity as complexly organized as the human brain. He is more impressed with the part played by the innate inherited structure of embryonic cells than that which metabolic gradients or the like may play in development. Localized centers of high metabolic rate have been demonstrated in eggs and embryos (Child and others) and no evidence is presented that makes untenable the theory that gradients are the integrating factor in development.

The material is admirably presented and the English is good. In these days of supernaturalism in Europe it is most gratifying to see not only meticulous care in the assigning of credit to others but often a gracious appreciation of achievement.

**Parasitology, with Special Reference to Man and Domesticated Animals.** By Robert Hegner, Ph.D., Professor of Protozoology, The Johns Hopkins University, Francis M. Root, Ph.D., Donald L. Augustine, Sc.D., Assistant Professor of Helminthology, Harvard University, and Clay G. Huff, Sc.D., Associate Professor of Parasitology, University of Chicago. The Century Biological Series, Robert Hegner, Editor. Second edition of "Animal Parasitology." Cloth. Price, \$7. Pp. 812, with 308 illustrations. New York & London: D. Appleton-Century Company Incorporated, 1938.

This is a second revised edition of *Animal Parasitology* (1929) under a different title to remove the impression that the book was devoted primarily to the parasites of animals other than man rather than primarily to those of man and his domesticated animals. The same authors are retained with the addition of Professor Huff to supplement the work of the late Prof. Francis M. Root on Arthropods of Parasitological Importance. Professor Hegner writes the introduction on parasitism and the protozoology, Professor Augustine the helminthology. The entire text and the bibliographies have been brought down to date and new illustrations added. The book meets the needs of physicians, veterinarians, and teachers and students of human and veterinary parasitology.

**La syphilis du système nerveux: Pathologie générale, thérapeutique et prophylaxie.** Par A. Sézary, professeur agrégé à la Faculté de médecine de Paris. Paper. Price, 48 francs. Pp. 287, with 28 illustrations. Paris: Masson & Cie, 1938.

This is written in simple and concise language and is mainly the result of the author's rich experience in the past thirty years. It is divided into five parts. The first part discusses spinal fluid examinations and syphilitic meningitis. The second part discusses possible etiologic factors such as neurotropic virus, environment and the role of treatment in late nervous complications. The third part concerns itself with pathogenesis of the two great classes of nervous disorders, mainly vascular and parenchymatous nervous syphilis, and is well treated. The fourth part deals with treatment and includes drugs, treatments of specific entities and complications. The fifth part deals with

prophylaxis of syphilis of the nervous system. The laboratory examinations receive adequate discussion. Illustrations are easy to understand, being semidiagrammatic. In the treatment the value of neoarsphenamine and bismuth compounds is generally recognized, especially in the prophylaxis of nervous syphilis. In the specific treatment of dementia paralytica, acetarsone alone has been used quite extensively and the author feels it has given as good results as malaria therapy. Tryparsamide is mentioned but not discussed. The methods of malaria therapy and other means of fever therapy such as typhoid, foreign protein and electrohyperpyrexia are not discussed. Although the book does not cover the various treatments of central nervous system syphilis it is a valuable addition to the practitioner's library.

**Bile: Its Toxicity and Relation to Disease.** By O. H. Horrall, M.D., Ph.D., F.A.C.S., Department of Physiology, the University of Chicago. Cloth. Price, \$4. Pp. 434. Chicago: University of Chicago Press, 1938.

This monograph endeavors to summarize and analyze the physiologic and toxic actions of bile as revealed by "past observations and experiments." The author has made an exhaustive study of the literature dealing with the history of bile and a study of its constituents, toxicity and effect on various parenchymatous organs of the body. Three chapters are given to a study of bile and its relation to icterus. A bibliography of 2,177 references forms a valuable part of the book; in the preface it is stated that, because "it is intended to conserve the time and labor of workers in this field, only the more significant publications have been included." The book is comprehensive and should be of great interest to all workers in the field of hepatic diseases and disturbances, both clinical and experimental.

**The Big House of Mystery: A Physician-Psychiatrist Looks at Ten Thousand Crimes and Criminals.** By Patrick H. Weeks, M.D., Physician and Psychiatrist, Indiana State Prison. Cloth. Price, \$2. Pp. 259, with 5 illustrations. Philadelphia: Dorrance & Company, 1938.

The author is physician and psychiatrist to the Indiana State Prison. He presents his work not as a scientific treatise on crime but as a record of the way in which modern criminology handles the criminal. He tells his story as a series of records of notorious criminals with whom he has been in contact. Obviously the most important of them was Dillinger.

**Papers on Psycho-Analysis.** By Ernest Jones, M.D., M.R.C.P., President of the International Psycho-Analytical Association and of the British Psycho-Analytical Society. Fourth edition. Cloth. Price, \$8. Pp. 643. Baltimore: William Wood & Company, 1938.

This is the fourth edition of the collection of the Jones essays. In the present edition the author has omitted twenty old papers and inserted twelve new ones. Once this work was well nigh a presentation of all the freudian concepts. Today many of the freudian school have minor disagreements with the freudian concepts and have some new ideas of their own which have not proved acceptable to Professor Freud himself. These are also reflected in Dr. Jones's book. His ability to present his material in easily readable language and his sincere earnestness in relationship to the subject make him a leader in his field and well worthy the attention of the average physician.

**Zum Krebsproblem und verwandten Gebieten: Infektion, Regeneration, Zellmutation, Befruchtung.** Von Dr. Fritz Niedermayer, Chefarzt und Leiter der Chirurgischen Abteilung des Krankenhauses Passau. Paper. Price, 5 marks. Pp. 166. Leipzig & Vienna: Franz Deuticke, 1938.

Cancer is produced by "bastard" cells that result from the union of epithelial and connective tissue cells, or their chromosomes, with cells of the reticulo-endothelial system. Other views of the origin of cancer are considered, as are also its relation to biocatalysis, phagocytosis and infection, including virus diseases. In the author's experience malaria and exophthalmic goiter hinder the development of cancer, owing he believes to the circumstance that in these diseases there is an increased lymphocytic activity which is held to be the most important anticancer influence in the body. A report on the effect of inoculating exophthalmic tissue into cancer will be published later. While the first essential in the treatment of cancer is early diagnosis and prompt removal or destruction of the cancerous growth, measures to promote harmonic and catalytic



processes are advisable in all stages of the disease. For this purpose are recommended organ extracts, notably of the spleen and the embryonal liver, copper, arsenic, terpenes and intestinal disinfectants, but no definite courses of treatment are prescribed and no clinical results are detailed. The discussion is speculative and inconclusive. The author published a book in 1936 on the cancer problem, to which he refers frequently in this volume.

**Aids to Bacteriology.** By William Partridge, F.I.C. Sixth edition revised by H. W. Scott-Wilson, B.Sc., B.M., B.Ch., Director of the Laboratories of Pathology and Public Health, London. Cloth. Price, \$1.50. Pp. 300. Baltimore: William Wood & Company, 1938.

Since the last edition the original author, William Partridge, has died. The sections concerning streptococci, the coli-typhoid groups, Neisseria and the filtrable viruses have been revised. This little pocket edition should be quite useful to workers in the diagnostic laboratories.

## Bureau of Legal Medicine and Legislation

### MEDICOLEGAL ABSTRACTS

**Hair Dyes: Dermatitis Attributed to Use of Dye.**—The plaintiff, the owner and operator of a beauty parlor, purchased a hair dye known as Roux Shampoo Tint from an agent of the defendant, the Roux Distributing Company, a distributor for the manufacturer, the Roux Laboratories, Inc. Following the use of the hair dye on a customer, the plaintiff developed a dermatitis of her face, hands and arms. The skin over the areas involved was raised and swollen. She suffered such severe pain that she was unable to carry on her business or even do her household work. She sued the defendant, alleging that the dermatitis was due to a poisonous substance in the hair dye. The trial court rendered a judgment in her favor, the court of appeals, Cuyahoga County, Ohio, reversed that judgment and the record was certified to the Supreme Court of Ohio for review.

The buyer of a product, said the Supreme Court, not only has a contractual right that the product will be as warranted and will be fit for the particular purpose intended but the further common-law right not to be harmed or injured by some unknown or hidden ingredient or defect when the product is used in the manner intended. If the product sold is unfit for the use intended, there has been a breach of warranty, express or implied. If the buyer is injured because of some unknown dangerous ingredient in the product purchased, then there has been negligence. Circumstances may be such that both a breach of warranty and negligence exists. In the instant case the evidence showed that the hair dye was not only unfit for the purpose intended but also contained a poisonous ingredient, unknown to the plaintiff, which in the use of the product on a customer injured the plaintiff. There was undisputed medical testimony that the dermatitis had been caused, not by a "supersensitivity," but by a poison in the preparation. The plaintiff was entitled to introduce evidence tending to prove either breach of implied warranty or negligence and the trial court did not err in submitting the case to the jury on the issue of negligence.

No error was committed by the trial court in permitting a chemist to perform a "so-called experiment" while testifying. The witness, who had had many years of experience as a chemist, in order to illustrate the action of hydrogen peroxide, placed his finger in a high concentrate solution of hydrogen peroxide (100 volume), removed it from the solution and showed the jury how it was whitened and then placed his finger in a glass of water. This testimony was admitted in connection with other evidence of the chemist with respect to the effect of the hair dye in question on the human skin. There was no claim made that the witness was not a qualified chemist.

The Supreme Court reversed the judgment of the court of appeals and affirmed the judgment of the trial court in favor of the plaintiff.—*Sicard v. Kremer (Ohio)*, 13 N. E. (2d) 250.

**Workmen's Compensation Acts: Action at Law Not Maintainable for Disease Not Compensable Under Act.**—Murphy, in using a spray gun for painting in the course of his employment with the American Enka Corporation, inhaled fumes of turpentine and other chemical elements in the paint. Eventually an abscessed kidney developed, which permanently and totally disabled him. He was denied compensation under the workmen's compensation act of North Carolina, the industrial commission finding that his disability resulted neither from an injury by accident in the course of his employment nor from any of the occupational diseases made compensable by the act. The superior court, Buncombe County, affirmed the judgment of the commission, and the workman did not appeal further. Instead he instituted a common law action for damages against the employer and one of its foremen. The trial court, in effect, dismissed the action, and the plaintiff appealed to the Supreme Court of North Carolina.

The plaintiff and the defendant employer, said the Supreme Court, having accepted the North Carolina workmen's compensation act, are bound by its provisions. The act originally defined "injury" and "personal injury" for which compensation is allowable to "mean only injury by accident arising out of and in the course of the employment, and shall not include a disease in any form, except where it results naturally and unavoidably from the accident." Thereafter the legislature in 1935 extended the provisions of the act to cover named occupational diseases. The workman conceded that the injury of which he complained was not an occupational disease named in the 1935 amendment. He contended, however, that the statutory definition of the word "accident" eliminated his injury from the provisions of the compensation act and that a common law action against his employer would lie for actionable negligence. With this contention the Supreme Court disagreed, citing *Lee v. American Enka Corp.*, 212 N. C. 455, 193 S. E. 809, in which it was said:

When the plaintiff in this action failed to reject the North Carolina Workmen's Compensation Act, as applicable to his employment by the defendant, American Enka Corporation, and thereby became subject to its provisions, in consideration of the liability assumed by the said defendant to pay to him compensation for an injury which he might suffer by an accident arising out of and in the course of the employment, without regard to whether the accident and resulting injury were caused by its negligence, he surrendered his right to recover of the defendant damages for an injury caused by the negligence of his employer, and waived his right to maintain an action in the superior courts of this state to recover such damages.

For the reasons stated the judgment of the trial court dismissing the action was affirmed.—*Murphy v. American Enka Corporation (N. C.)*, 195 S. E. 536.

**Accident Insurance: Arrested Arthritis Not a Disease.**—The defendant insurance company issued a policy on the life of Upchurch providing double indemnity if death resulted "directly, and independently of all other causes, from bodily injury . . . effected directly through external, violent, and purely accidental means . . . and not caused by or contributed to, directly or indirectly, or wholly or partially, by any disease." In 1934 Upchurch had arthritis in his left ankle and left knee, which lasted four or five days. Thereafter he seems to have completely recovered; he was not sick, he lost no time from his work as a traveling salesman and he indulged in physical exercise such as cultivating a garden. Dec. 1, 1936, he fell down a flight of steps and injured his left knee and left ankle. He was able to get about for several days but pains developed in both legs and in his back. His attending physician diagnosed his ailment as acute arthritis. On December 23 he died. The insurance company denied liability under the double indemnity clause and Upchurch's beneficiary, his widow, brought suit against the company. The jury returned a verdict in her favor and when the trial court refused to order a new trial the insurance company appealed to the court of appeals of Georgia, division 2.

The sole question before the court of appeals was whether the evidence was sufficient to justify the jury in finding that the death resulted proximately from a bodily injury of the character described in the double indemnity clause and not from

a disease. Medical witnesses testified that the arthritis from which the insured died developed from germs of the disease which were in his system prior to his injury, that the germs of arthritis could be encapsulated in a person's body, or be dormant, and the person would not suffer from the disease, and that the physical injuries which the insured received from the fall caused the encapsulated or dormant germs of arthritis which were in his system to flare up and develop the disease. This evidence, in the opinion of the court, was sufficient to justify a finding by the jury that the insured did not have arthritis or any other disease prior to the fall, and that the arthritis which developed after the fall was directly caused by the injury.

The judgment in favor of the widow was affirmed.—*National Life & Accident Ins. Co. v. Upchurch (Ga.)*, 195 S. E. 588.

## Society Proceedings

### COMING MEETINGS

American Academy of Orthopedic Surgeons, Memphis, Tenn., Jan. 15-19. Dr. Carl E. Badgley, 1313 East Ann St., Ann Arbor, Mich., Secretary.  
American Association for the Study of Neoplastic Diseases, Baltimore, Dec. 28-30. Dr. Eugene R. Whitmore, 2139 Wyoming Avenue N.W., Washington, D. C., Secretary.  
American Student Health Association, New York, Dec. 29-30. Dr. Ruth E. Boynton, Students Health Service, University of Minnesota, Minneapolis, Secretary.  
Eastern Section, American Laryngological, Rhinological and Otolological Society, Boston, Jan. 11. Dr. Frank E. Kittredge, Masonic Temple, Nashua, N. H., Chairman.  
Middle Section, American Laryngological, Rhinological and Otolological Society, Sioux City, Iowa, Jan. 19-20. T. R. Gittins, Davidson Bldg., Sioux City, Iowa, Chairman.  
Southern Section, American Laryngological, Rhinological and Otolological Society, New Orleans, Jan. 14. Dr. Francis E. LeJeune, Maison Blanche, New Orleans, Chairman.  
Southern Surgical Association, White Sulphur Springs, W. Va., Dec. 6-8. Dr. Alton Ochsner, 1430 Tulane Ave., New Orleans, Secretary.

### THE AMERICAN RHEUMATISM ASSOCIATION

*Fifth Annual Meeting and Seventh Conference on Rheumatic Diseases, held in San Francisco, June 13, 1938*

LORING T. SWAIM, M.D., Boston, Secretary

(Concluded from page 2044)

#### Neurologic Symptoms and Clinical Observations in Patients with Cervical Degenerative Arthritis

DRS. STACY R. METTIER and CHARLES S. CAPP, San Francisco: The present study was undertaken to analyze the symptoms suggestive of cervical nerve root origin occurring in patients presumably having osteo-arthritis, and to attempt to correlate these symptoms with roentgenograms of the cervical vertebrae taken in the anteroposterior, lateral and oblique projections. The series consisted of thirty patients. Most of the patients were between 40 and 60 years of age. Three were under 40 years of age.

The symptoms complained of most frequently were pain, rigidity of the neck and muscular weakness of the hand or arm. In their general character and distribution the symptoms were uniform enough to lead one to suspect the presence of a common underlying pathologic process. Such, however, was not the case in our experience. Hypertrophic changes were observed in eighteen cases. These consisted of circumferential osteophyte formation which projected into the intervertebral canals. These were well visualized in the films taken in the oblique projections. In addition, in the involved regions there was slight narrowing to almost complete obliteration of the intervertebral spaces. The sites of predilection were between the fifth and sixth and the sixth and seventh cervical vertebrae. In seven cases there were similar symptoms but the roentgenograms showed only a minimal amount of osteo-arthritis. Narrowing of the intervertebral disks occurred in only three cases. In four cases presenting symptoms of radiculitis there was no apparent abnormality of the articular facets in the roentgenograms, no evidence of proliferative new bone formation at the margins of the vertebrae,

no noticeable narrowing of the intervertebral foramina and no thinning of the intervertebral disks.

This syndrome of pain and muscular stiffness about the neck and in the shoulder girdle or the radiation of pain down the arm is of relatively frequent occurrence in persons beyond 40 years of age. From our studies it was learned that in approximately two thirds of the cases there was roentgenologic evidence of hypertrophic arthritis. In the remaining cases there was no evidence of arthritis or of any other pathologic process in the x-ray films. The value of taking x-ray films in the oblique projection is emphasized. The patients were greatly relieved of their symptoms by the application of heat, massage, manual traction and manipulation, and posture training.

### DISCUSSION

DR. NEVILLE T. USSHER, Santa Barbara, Calif.: The authors ask us as internists to make a diagnosis in a field ordinarily relegated to the orthopedic department. The radicular syndrome for some time has been stressed chiefly by orthopedists and neglected by those who look for visceral pathologic conditions to account for referred external pain. In my experience degenerative changes in the cervical spine are but one factor in the production of referred pain to the occiput, shoulder girdle and precordium. Often a cervical lordosis or a scoliosis with angulation at the seventh cervical vertebra is enough to produce severe referred symptoms quite distant from the actual point of irritation. Actually these curvatures are often the prime etiologic factors in producing the degenerative changes in the vertebra. Orthopedists stress the importance of the wear and tear on the articular surfaces in producing such arthritides, and it is the malposition of weight-bearing surfaces due to these curvatures of the spine that increase this wear and tear element. The effect of cervical pathologic changes on the autonomic nervous system is important and yet insufficiently recognized. Recently in Santa Barbara I have demonstrated in a number of cases the relation of severe "sphenopalatine pain" (as described by Sluder) to disturbances in the cervical spine. Correction of angulations in this area by postural exercises or by heel raises for example have resulted in striking relief of symptoms. This "deep facial" pain is definitely associated with the sympathetic network and I feel that it cannot be explained on the basis of damage to the cervical somatic nervous system. The cervical somatics can and do take part in hyperesthesia and pain of the scalp and external facial structures but apparently do not influence typical sphenopalatine pain. My observations suggest that damage to the cervical spine and surrounding tissues over a long period may result in trophic changes of the mucous membranes of the nose and possibly may affect intra-ocular tension or muscle balance. Whether tinnitus and lessened acuity of hearing due to sympathetic irritation of the auditory apparatus is another feature I am not able to state definitely. At any rate further study of these observations is indicated. It is evident then that degenerative as well as other structural changes in the cervical spine have more effect on the body economy than has been ordinarily realized.

DR. LEWIS GUNTHER, Los Angeles: In 1893 a Russian by the name of van Bechterew published, in German, a description of the arthritic changes in the spine now known by his name and described the associated radicular muscle atrophies and sensory disturbances. Until 1928, when the description of radiculitis associated with hypertrophic osteo-arthritis of the spine by Dr. Kerr and myself appeared, the term radiculitis had been used with only a few exceptions to describe the acute sensory (and sometimes motor) disturbances such as Dejerine described in relation to syphilis of the nerve roots. The few references to the subject were by Camus in 1907, Leri in 1916, Sicard in 1918, Rosenheck in 1924 and Nielson in 1927. None of the articles, until our descriptions in 1927 and 1928, had a composite picture of the syndrome sufficient for an accurate differential diagnosis. The sufferer from arthritis of the spine has symptoms which are both objective and subjective. The subjective symptoms of radicular sensory disturbances are as accurate and of as much diagnostic importance as are the objective observations. The former can be obtained accurately during the history taking but the latter are sometimes difficult to demonstrate.

Because of the rarity of references to the neurologic complications it was our problem to prove that hypertrophic osteoarthritis of the spine could cause pain and that this pain was a variety of radiculitis. It is interesting to have heard Drs. Mettier and Capps say "we can look at the x-ray film and predict where the patient has his pain." In those days Dr. Kerr and I studied the patient's symptoms and sensory alterations and tried to predict which vertebrae would show the pathologic changes. We were able to show that there were subjective and objective sensory disturbances. These had the well defined anatomic pattern of the radicular or segmental distribution of the dermatomes of the body. We were able to demonstrate either increased or decreased sensation to the pinpoint, to the cotton tuft and to pinching the skin. Always these disturbances showed the segmental distribution. Hyperesthesia was usual when the symptoms were of recent onset. In the older patients hypo-esthesia was present throughout the entire root distribution, either unilateral or bilateral. Muscle spasms were also observed in the acute phases and muscle atrophies in the patients with symptoms of long standing. The motor disturbances were likewise of a nerve root pattern, involving muscles or groups of muscles supplied by the particular spinal nerve root or roots. In old arthritis of the lowermost cervical vertebrae we found atrophy of the thenar or hypothenar eminences. The subjective symptoms consisted of pain, aching and paresthesias, described accurately by the patient in a half or full segment covering one or more nerve root distributions. The paresthesias described as burning, numbness or tingling were of particular significance in the differential diagnosis. Paresthesias were common symptoms of root pain and were uncommon in the symptoms of visceral pain referred by way of the same nerve roots. So accurate are the topographic descriptions of the patient during the acute phases of his symptoms that one might think he had read a textbook on neuro-anatomy.

In my experience there is absolutely no quantitative relation between the amount of x-ray evidence of bony changes to the degree of symptoms. The first descriptions of radiculitis by Dejerine's pupils was of an acute process of syphilitic origin in which there were no bony changes. Herpes zoster, another manifestation of a true subjective as well as objective radiculitis, may have no relation to vertebral pathologic conditions. One might see tremendous evidence of bony involvement by means of the x-rays and witness no subjective symptoms. It is often difficult to differentiate clearly the origin of pain in the epigastrium, in the right lower quadrant, across the lower abdomen, or across the shoulders and down the outer sides of the arm and forearm. However, if the complete segmental distribution of pain of radicular origin is kept in mind, in contradistinction to the spotty zones (Head zones) occurring within parts of segments seen in visceral referred pain, the origin of any painful symptoms will be explained. Many pathologic processes in the spine may cause nerve root symptoms. Whether it is bony excrescences protruding into and decreasing the size of the intervertebral foramina, as Drs. Mettier and Capp have pointed out, or exudate as shown by Nathan in his experiments, or hypertrophic granulations, or scoliosis as pointed out by Dr. Ussher's discussion, tumors of the vertebrae or the meninges, tuberculosis or syphilis of the nerve roots as originally shown by Dejerine and his pupils, or involvement of the roots at the rib articulations as shown by Dr. Kerr, the symptoms at the periphery will be of one topographic distribution, namely segmental according to the dermatomes of the body.

The second cervical nerve root covers the scalp area from the occiput to the vertex and extends downward over a small area in front of the ear and over the posterior portion of the mandible. Most of the ear is supplied by the cranial nerves. The fourth cervical nerve root supplies the entire area of the shoulder from the second interspace in front to the spine of the scapulae behind and laterally to the surface markings of the deltoid muscle. There are two areas in this region which are not supplied by this root: The area between the surface markings of the sternomastoid muscles on the sides and front of the neck is supplied by the third cervical nerve root and the triangular area up and down the back of the neck, which has its apex at the occiput in the midline and its base approximately

at the level of the spines of the scapulae and delineated laterally by the surface markings of the deltoid muscles. This triangular area is supplied by the fifth, sixth, seventh and eighth cervical (and sometimes by the first dorsal) nerve roots. In addition to the triangular area over the back of the neck, the fifth to eighth cervical nerve roots also distribute down the outer side of the arm and forearm and to the fingers. The fifth cervical nerve root supplies the outer half of the arm from the area of the deltoid muscle to the external condyle of the humerus. The sixth cervical nerve root supplies the outer or radial half of the forearm including the thumb and first two fingers. The seventh cervical nerve root supplies part of the second and third fingers. The eighth cervical nerve root supplies the fourth and fifth fingers and the ulnar half of the forearm to approximately the inner condyle of the humerus. Here the eighth cervical nerve root lies adjacent to the first dorsal nerve root, which supplies the lower and inner half of the arm, the second dorsal root, supplying the upper half, and the third dorsal nerve root the armpit area. I wish to call attention particularly to the deltoid to thumb distribution of the upper extremity, which is supplied by the fourth, fifth, sixth and seventh cervical nerve roots in contrast to the armpit to little finger distribution, which is supplied by the third, second and first dorsal nerve roots. It is these two areas that come into consideration in the differential diagnosis of referred pain from the heart. Either area can be painful from arthritis of the cervical spine and upper dorsal vertebrae, but angina pectoris, or pain referred from the heart, confines its distribution from the armpit to the little finger area, and rarely from the deltoid to the thumb distribution of these dermatomes. Pain of nerve root origin involves the entire distribution of the dermatomes at least unilaterally, whereas referred heart pain occurs in areas within several of the nerve root distributions, covering or overlapping parts of two or more dermatomes without completely covering the entire distribution of the particular roots. Similarly, arthritis of the third and fourth cervical vertebrae will involve the entire distribution of the shoulder area and the side of the neck, whereas pain referred from the heart occupies only small areas (Head zones) within the entire dermatome.

The diagnostic picture presented is not difficult to obtain if a little effort is expended in obtaining an exact understanding of the language used by the patient. The borders of the dermatome will be accurately shown if you ask him to indicate how far down the pain reaches on the front and back of the chest and on the sides of his shoulder. In a similar way, when the fifth, sixth, seventh or eighth nerve roots are involved, radiation to the dermatomes on the outer sides of the extremities will be indicated as well as the area up and down the back of the neck. He will differentiate accurately the difference between the deltoid to thumb areas of cervical vertebrae disorder as against the armpit to little finger radiation seen in involvement of the upper dorsal vertebrae. By his descriptions he will also differentiate between the spotty (Head zone) distribution of referred heart pain and the complete area of the dermatome seen in radicular pain.

When the patient is questioned carefully on the sequence of symptoms in relation to activity, the following type of story is apt to be heard: Symptoms begin in the morning when the patient gets out of bed. He usually eases himself over the side because it is painful to sit up abruptly or to jump out of bed. The extremities feel stiff, and the hands and fingers are apt to be stiff or feel swollen. Usually by the time the morning ablutions are completed there is less pain, but shortly after the breakfast hour, when the day's physical activities have begun, symptoms return. Straining at the stool, yawning, sneezing or coughing will induce symptoms. The housewife may be annoyed sufficiently to find it necessary to lie down. She gets some relief, but her pain returns soon after she has relaxed and forces her into activity again because she gets relief by moving around. But after a while fatigue and pain return. That is the painful program of the day. If she uses her car a bumpy road aggravates her pain, or if she "misses a step" it brings on acute symptoms. At bridge or in the theater she shifts her position frequently. By bedtime the patient is thoroughly worn out, irritable and full of annoying aches and pains which have hardly ceased during the entire day. But the pain does not leave her

and she soon awakens. Shifting her position in bed affords some relief but an uninterrupted night's sleep is unknown to her. However, considerable comfort at night can be had by placing boards under the mattress or by the use of an ordinary pad mattress and a simple wire mesh support which is relatively nonyielding and gives support to the vertebral column muscles during sleep. The patient not infrequently takes the mattress from the bed and places it on the floor and there finds sufficient comfort for a peaceful night. This is the picture of the sufferer from hypertrophic osteo-arthritis of the spine.

DR. M. J. SHAPIRO, Minneapolis: Roentgenograms of a group of patients between the ages of 40 and 60 complaining of pain in the back of the neck will reveal a good many with evidence of osteo-arthritis in the spine. Before one makes a diagnosis of radiculitis it is most important to understand that many normal persons have osteo-arthritic changes in the cervical spine. It is not nearly as difficult to make this diagnosis if the dorsal spine is involved. I should like also to ask the authors whether they don't find this syndrome much more common in women—especially during the menopausal period—and whether or not this condition is not a self-limited disease. I have seen a number of patients with radiculitis and a lot of pain and after a number of months or years the whole thing disappears. Why is it that so many persons with extensive osteo-arthritis of the spine have no symptoms of radiculitis?

DR. K. K. SHERWOOD, Seattle: There is one point that has not been emphasized in these discussions about radiculitis and that is the physical examination of the patient. Frequently the differential diagnosis lies between visceral disease, intrinsic nerve disease and external pressure on the nerve. If the disease is due to pressure on the nerve where it emerges from the spinal canal, decreasing the size of that opening should increase the symptoms. This can be done simply by lateral flexion of the neck. Thus if that motion increases the pain one can say that the pain is due to pressure which is exaggerated by decreasing the size of the foramina. On the other hand, in the intrinsic nerve diseases lateral flexion will relieve the pain, whereas extending the lateral flexing of the neck from the opposite direction will increase the pain. I found this to be of value in the diagnosing of this radicular syndrome. Further, I believe that the importance of the x-rays is more in prognosis than in diagnosis.

DR. CHARLES S. CAPP, San Francisco: We purposely eliminated those cases in which there was any scoliosis or patients with extreme cervical lordosis, who project their neck far forward because of their myopia in the attempt to see better. We examined many more than forty cases, but we are trying to group those which had no other demonstrable pathologic lesions. With regard to myositis as a possible cause of pain, in some of our cases, but not in all, blood sedimentation studies were made, and in none of them did we find evidence of inflammation as indicated by increased sedimentation rate. I cannot eliminate fibrositis as a possible cause of symptoms, for we haven't taken biopsy specimens of the connective tissue or muscle. Women had symptoms in the ratio of 60 to 40 per cent to men. Frequently relief could be given women by proper support of pendulous breasts, by correcting posture or by proper use of the muscles comprising the shoulder girdle. By fluoroscopy one can determine the amount of movement of the cervical spine. If there is a narrowing of only one intervertebral disk there is no limitation of motion of the spine in flexion or extension except at the disk in question. There is definite limitation of motion if two or more disks are narrowed. Flexion narrows the intervertebral canal aperture and extension opens it. The x-ray demonstration of bone proliferation at the intervertebral disk margin is a late manifestation of the disease process. We are trying in our pathologic studies on autopsy material to correlate the presence of roentgen observations with previous clinical symptoms and to follow the progression of the disease process by clinical and x-ray studies on ambulant patients at stated time intervals.

DR. WILLIAM J. KERR, San Francisco: I have been much interested in one particular group of patients who have a pain in the cervical region, particularly those who are obese, with a large and pendulous abdomen, who lean backward to keep from

falling over. They stoop as if they were going into a tunnel. Many of these patients complain of pain in the back of the neck radiating to the side, to the occipital region or, sometimes, to the shoulders until relieved by postural correction or by dietary measures. In the ordinary relaxed position they have pain; if the abdomen is supported or if they stand erect the pain is immediately relieved. I don't know the mechanism of relief unless it is the change in the size of the foramen or perhaps the relaxation of the ligaments under strain.

### The Synovial Membrane

DR. DAVID H. KLING, Los Angeles: Since the latter half of the nineteenth century the view has been held that the synovial membrane is merely a modified connective tissue devoid of special function. The synovial fluid was therefore regarded as a transudate, or a product of degeneration of the synovial lining or cartilage. Recent investigations, however, contradict this concept.

The most striking feature of the synovial membrane is the great difference in structure of neighboring areas. This is well shown in the lantern slides of a systematic method of dissection of the human knee joint. By a modified toluidin blue stain I have demonstrated metachromatic mucin granules in the cytoplasm of synovial cells, chiefly in the villi of the infrapatellar fat pads, and in the fornix, and only occasionally in the popliteal pouch. In the areas where the lining appeared tendinous, as in the lower part of the anterior aspect of the suprapatellar bursa and in parts of the lateral sides of the lining, no secretory synovial cells were found. The secretory cells were large and polygonal with a dark bluish nucleus and red metachromatic granules.

Later, Vaubel demonstrated marked polymorphism of synovial cells in tissue cultures. He confirmed the finding of metachromatic granules in the cytoplasm when using the toluidin blue stain. King demonstrated readily a Golgi apparatus in the synovial cells of normal human synovial tissue. It was absent in degenerating cells. This is a further proof that the synovial cells, which elaborate mucin, are healthy and active, and that the synovial fluid is not a product of degeneration.

These studies have led to the conclusion that the structure and function of the synovial membrane is twofold; it consists of a connective tissue sleeve in which secretory elements are interposed for the elaboration of synovial mucin. Corresponding to the difference in structure of the synovial membrane are also differences in the interchange of solutions, colloids and particles between the synovial membrane and the circulatory and lymphatic systems. The fibrous areas are capable only of absorption of molecular solutions, e. g. iodides or phenosulfonphthalein from the joint cavity at a rate corresponding to the absorption from tissue spaces. The villi and cell-rich areas contain cells which are able to take up colloidal suspensions from the circulation. Some synovial lining cells store particles of inert or reactant material. The reaction of the synovial tissue to irritation and inflammation is twofold. First there is the general reaction of the mesenchymal tissue, which consists of changes in the circulation, dilatation of blood vessels, extravasation of plasma and migration of leukocytes and later of macrophages from the circulation as well as from the tissues. The irritation provokes an increased activity and the production of larger amounts of synovial mucin. I found mucin in more than 95 per cent of all traumatic and inflammatory effusions. In turn, this hyperactivity causes a hypertrophy of the synovial lining cells. The highest degree is seen in conditions of milder irritations of prolonged duration which do not lead to destruction of the synovial membrane. The extent of the primary destruction and the subsequent reaction of the tissues varies according to the severity of the damaging agent. In septic, purulent arthritis and in severe cases of gonococcal and tuberculous arthritis, large parts of the synovial lining are destroyed in toto. No hypersecretion is possible because the secretory areas are wiped out. In less severe types, both general inflammatory reactions and hypertrophy of the synovial cells are present. In these types, joint effusions are common. Besides noncharacteristic inflammatory processes, we see in the synovial lining granulomatous formations, more or less typical of certain diseases, such as rheumatic nodules, tubercles or gummas.

## DISCUSSION

DR. J. ALBERT KEY, St. Louis: Dr. Kling's paper gives the impression that there are in the synovial lining of joints certain cells which are specifically devoted to the formation of mucin. That is something which people have been trying to prove for a good many years and dates from the time when Havers described mucin cells in joints. I have never been able to persuade myself that there was such a specific cell in the synovial surface under any conditions. I have always rather objected to the term synovial membrane because I feel that the synovial surface is not a true membrane but is simply a fault in the connective tissue on which cells have accumulated and that the structure of that surface, just as Dr. Kling has said, varies with the mechanical forces to which it is subjected. It doesn't make any difference what part of the body is subjected to friction—a bursa will form, that bursa will contain synovial fluid, and that fluid will contain mucin. If one removes the synovial membrane from the joint as completely as one can remove it, another synovial membrane will form, not by the outgrowth of specific cells from the edges of the defect but by the change of the cells *in situ*, and connective tissue cells that are left will proliferate and form a new surface. Also if a false joint is created by doing an arthrodesis, or if a false joint is created in a nonunion, a synovial surface will develop to line the cavity. With regard to absorption, the more deeply an animal is stained with trypan blue or other colloidal dye, the more numerous will be the cell elements which will take up that dye. For instance, if an animal is stained deeply enough even the cartilage cells will take up trypan blue. Also the macrophages are constantly wandering back and forth through the synovial membrane into the joint and out of the joint and they are one of the most important factors in distributing infection into the joint from the surrounding tissue and in eliminating foreign material, including bacteria, from the joint.

DR. JOHN SAUNDERS, San Francisco: I am happy to hear Dr. Key emphasize the fact that the so-called synovial membrane is not strictly a membrane. In this instance the term "membrane" is definitely a misnomer. It has not been sufficiently appreciated that the synovial lining of any one joint presents well defined differences of morphology in different regions of the same joint. The existence of these differences has led to many erroneous conclusions in the interpretation of histologic appearances both in health and in disease. I am entirely unconvinced as to the existence of specific secretory cells in the synovial membrane, as is contended by Dr. Kling. The evidence presented so far seems inadequate to establish such cellular specificity and does not fulfil those criteria whereby we recognize secretory activity elsewhere. There is as yet no irrefutable evidence that these cells constitute a part of the mechanism for the elaboration of the synovial fluid. Frankly I am unable to discover any difference between the so-called specific cell and the macrophage. In this connection one should keep in mind that the synovial membrane is essentially a mesothelial structure. The view that the synovial fluid is the product in part of transudation of serum from the vessels of the synovia and in part from the destruction of the articular cartilage has much to commend it. The work of MacConaill on the circulation of the synovial fluid deserves wider recognition because of its fundamental nature. This author has emphasized the importance of incongruity of joint surfaces and of the degree of viscosity of the synovial fluid for adequate lubrication of a joint. By reference to the theory of lubrication he has shown that the incongruity of joint surfaces established cuneiform spaces which create mechanical conditions enabling a positive pressure of the synovial fluid to develop between the opposed surfaces. In addition he has shown that the intra-articular cartilages of joints relate primarily to the synovial fluid, creating cuneiform intervals which assist in this process. The role of such cartilages is active rather than passive. MacConaill makes an interesting comparison between the menisci of the knee joint and the so-called Mitchell thrust pads. These thrust pads are a refinement of marine engineering employed when thrusts are to be carried by a film of lubricant during motions in which there is a considerable amount of gliding. Such pads or menisci increase in the higher ranges of motion the efficiency

of joints and their lubrication. It has been my custom to demonstrate this circulation and action of the interarticular cartilages to students. Goodsir pointed out in the 1860's that a joint must have incongruity—the worse the fit the better the joint, as it were. In this way only a small area is actually bearing at any one time, which allows of reconstitution of unapposed surfaces. MacConaill's work is a further elaboration of this principle. Dr. Key mentioned something about extra-articular fat simply filling up dead spaces about the joints. I object to this conception. I think it can be demonstrated that the fat plays an active rather than a passive part in joint mechanism. It should be remembered that fat is semifluid at body temperature. During movement there are changes in the capacity of a joint. Such changes in capacity permit the inward flow of the semifluid fat, which presses the synovial membrane, carrying with it synovial fluid, against the exposed surfaces of articular cartilage, lubricating them ready for the next movement. In no places can one demonstrate this functional mechanism more beautifully than in the action of the elbow or in the action of the knee joint.

DR. M. HENRY DAWSON, New York: Dr. Meyers, chemist of the Pathological Institute of the Medical Center, who has been studying the chemistry of synovial mucin, has been successful in isolating mucin in a pure form for the first time. It turns out to be not a nucleoprotein but a complex polysaccharide. This polysaccharide is not found as a normal constituent in the human serum. I believe that this will establish definitely and finally with no equivocation whatever that synovial mucin is a secretion and is not a transudate or degenerative product of cartilage.

DR. KEY: I think that this mucin is due to trituration of cells which are broken off from the surface.

DR. DAVID H. KLING, Los Angeles: Now Dr. Key and Dr. Saunders have said that they couldn't find these secretory cells. I want to ask them whether they have studied these cells with the toluidine blue stain?

DRS. KEY and SAUNDERS: No.

DR. KLING: There are others, including myself, who have studied these cells by toluidine blue and we have found mucin granules in the cells, and you will see them in my exhibit. I do not claim that the synovial membrane is a gland. I recognize the mesenchymatous origin of the synovial tissue. I do however claim that this tissue is pluripotent and contains non-differentiated cells which, under physiologic and pathologic stimuli, elaborate mucin. Such cells are also present in peri-articular tissue, and this explains the formation of bursa and ganglion after traumatic or inflammatory irritation. In two slides of a malignant synovial tumor the dual structure is pronounced. The connective tissue forms solid sarcomatous areas. The secretory cells, on the other hand, give rise to glandlike structures which are filled with mucin. Moreover, the metastases of this tumor in the lung show identical histologic pictures and thus support the conception of the dual nature of the synovial membrane.

## Gold Therapy in Proliferative Arthritis

DRS. J. ALBERT KEY, HERMAN ROSENFELD and O. E. TJOFALT, St. Louis: Seventy patients with arthritis of the proliferative type were treated with myochrysin (an aurothiomalate of sodium). Nine of them had spondylitis ankylopoietica and these were not appreciably helped by the gold compound. Of fifty-three patients with typical chronic atrophic arthritis with an average duration of over three years the results were as follows: Two became worse, six were not improved, four were slightly improved, thirteen were moderately improved, eighteen were markedly improved, three were apparently cured and seven were improved when last seen but did not return for a final examination. The gold compound was given at weekly intervals by intramuscular injections of from 0.025 to 0.1 Gm. of myochrysin until the patient received 2 Gm. of myochrysin (1 Gm. of gold). Then after a rest period of six weeks the treatment was resumed if the arthritis was still active. Toxic reactions were frequent and occurred in forty-four of the seventy patients. Most of the reactions were mild skin irritations but there were three cases of severe exfoliative dermatitis. There were no

fatal reactions. Vitamin C was given in excess during the treatment and patients with anemia were given liver or stomach extract and iron. Underweight patients were given a high caloric diet and overweight patients were given a low caloric diet. Gold therapy is dangerous and the patients must be watched carefully and the drug stopped at the first sign of a toxic reaction. It is believed that gold is the most valuable agent now known in the treatment of atrophic arthritis.

## DISCUSSION

DR. K. K. SHERWOOD, Seattle: I have used sodium gold thiosulfate for a period of four years in the treatment of certain forms of arthritis. I have used small doses, 10 mg., given intravenously at weekly intervals, until either the disease had ceased to be active, improvement ceased, or toxic signs developed. My results agree with Dr. Key's. Certainly, in the peripheral, true atrophic arthritis, it is beneficial in certain cases. I have at the same time run a control series in cases of an ambulatory character, using weekly physiologic saline placebos and I find that in this type of case approximately 25 per cent will remain stationary or get worse, while 25 per cent will spontaneously improve. Hence the 42 per cent of improved patients treated by Dr. Key and his co-workers with gold certainly indicates a definite therapeutic effect. All the severe reactions which I have seen occurred in the cases of spondylitis. Has Dr. Key found that spondylitis is especially apt to give trouble? My results agree with his in that there are no marked beneficial effects in cases of spondylitis. I am using a much smaller dose and getting approximately the same results. I wonder whether Dr. Key has tried a smaller dose, perhaps spread over a longer period of time. How frequently have routine laboratory tests, especially urine, hemoglobin, sedimentation and differential counts been made as a check on early signs of toxicity which do not give clinical manifestations? I have checked the blood in a routine manner every month.

DR. M. HENRY DAWSON, New York: The most complete report on the use of gold salts in the treatment of chronic arthritis is that of Hartfall, Garland and Goldie, published last year in the *Lancet*. In all, 750 cases of arthritis were treated, 590 of which were diagnosed as rheumatoid arthritis. These authors conclude that gold salts are the most effective therapeutic agents which we possess for the treatment of rheumatoid arthritis. However, they also report that toxic reactions developed in 40 per cent of the cases and seven fatalities due to the treatment are recorded. In a report from Australia, Parr and Shipton also report favorably on the use of gold salts. Seventy cases were treated with one fatality. We have not used gold therapy in our clinic simply because we were afraid to. If one patient out of every hundred succumbs to the treatment and 40 per cent have toxic reactions, it is obviously a dangerous form of therapy. One must be certain that the results justify the risks involved. It may be that further experience will show that such is the case. I should like to congratulate Dr. Key on his results in handling a potentially dangerous drug.

DR. PHILIP S. HENCH, Rochester, Minn.: I have just returned from a three months trip through England and Scotland. In those countries gold therapy is the form of treatment for atrophic arthritis which has elicited the greatest interest in the past ten years. It seems significant that interest in this treatment is still increasing, not diminishing. I discussed the merits and demerits of chrysotherapy with many physicians, among them Buckley, Copeman, Collins, Davidson, Goldie, Schlesinger and Tegner, as well as with Forestier and other continental physicians who were attending the International Rheumatism Conference at Oxford and Bath. I found that conservative internists and rheumatologists agreed that gold therapy, although somewhat dangerous, has produced better results in cases of atrophic arthritis than has any other single form of treatment or combination of treatments heretofore available. These men differed in their opinion on the incidence of toxicity from gold. Some noted toxic reactions of varying degrees in 40 per cent of those in which the treatment was used while others noted them in only about 10 per cent of cases. Most of the toxic reactions were of little significance. However, serious toxic reactions do occur in a small percentage of cases and in the series of 900 patients treated by Hartfall, Garland

and Goldie (*Lancet*, Oct. 2, 1937) a mortality rate of 0.8 per cent (about one in 125 cases) was ascribed to this therapy. Such a risk is much greater than that of any other form of antirheumatic treatment and places a serious obligation on the physician who chooses patients for such treatment. I believe that only those patients whose stubbornly progressive arthritis has resisted a thorough trial of the more orthodox and conservative therapy should be subjected to the treatment, at least until we in the United States have had more experience with it. The incidence of toxicity from gold has apparently been materially lowered the last two or three years by the use of doses smaller and more widely spread than those formerly employed. In general, the present program of treatment in England is to begin with small doses, injecting about 10 mg. at the first dose, either continuing with that dose two or three times or increasing subsequent doses at once to 25, 50 or 100 mg. A dose of 100 mg. is about the largest used. Injections are given about once a week till a total of 1 Gm. (occasionally 1.5 Gm.) has been given. This constitutes the first course. It is emphasized that nobody is cured or materially helped by one course alone. An interval of from ten to twelve weeks is allowed to elapse and then a second course is given. Sometimes three or even four courses are prescribed. "Cure" or marked improvement has been reported as occurring in from 70 to 85 per cent of cases. The treatment is not recommended in cases of atrophic spondylitis, hypertrophic arthritis or fibrositis. Great diligence must be used by physicians to note signs of impending serious toxicity and nobody should use this form of treatment without thoroughly familiarizing himself with such reports as those of Forestier (1935), Buckley (1936), Crosby (1936), Copeman and Tegner (1937) and particularly the report of Hartfall, Garland and Goldie (1937). Our English colleagues have accused us of neglecting to study a useful form of treatment; they believe that we too will approve of it when we have given it a "fairer" and much more extended trial than we have thus far.

DR. EPHRAIM GOLDFAIN, Oklahoma City: I began to use gold therapy as an additional measure in the treatment of chronic atrophic arthritis approximately five years ago. I use sodium gold thiosulfate in a stabilized solution. My routine procedure was to begin with 10 mg. of the gold salt intravenously, increasing the dose each week to where 50 mg. of the salt was being administered by vein each week. I found that that dose was too large and began reducing it to the point at which for a time I used an injection of 25 mg. of sodium gold thiosulfate intravenously at weekly intervals. Additional reports began to appear in the literature however about the desirability of using small doses of gold salts in other conditions. I then began to reduce the dose of gold salts and found that as good results were obtained and the likelihood of toxic reaction on the part of the patient was entirely obviated. I now administer the gold salts intramuscularly instead of intravenously. I find that given intramuscularly they cause no local reaction or induration. The dose given to the patient is 7.5 mg. twice a week so that a total of 15 mg. a week is being used. So far as I know there have been no deaths from the use of gold salts in accordance with the method thus outlined. I have not had any serious toxic reactions. Especially have I noticed that even mild cutaneous reactions are entirely obviated when the smaller doses last mentioned are being used. It is my observation and impression that the use of gold salts in the treatment of atrophic arthritis is of definite value and produces an increased percentage of improvement as compared to the treatment of these cases without gold salts. It is my feeling that gold salt therapy is an excellent addition to the armamentarium that we use in the treatment of these cases.

DR. R. GARFIELD SNYDER, New York: Dr. Key has carefully tabulated not only his successes but also his failures and his toxic reactions. He has warned us that gold therapy will not cure every case of chronic arthritis. It is my belief that gold therapy should not be used except in cases that have proved refractory to every other form of treatment. My associates and I have used gold therapy during the past three years in more than 200 cases in the Arthritis Clinic at the Hospital for the Ruptured and Crippled in New York, and in general our



results correspond closely to those obtained by Dr. Key and his co-workers. However, our results were not quite as good. This is probably due to the fact that Dr. Key used myochrysine, while we used sodium gold thiosulfate. European workers all agree that myochrysine is the most efficacious drug; it is also the most toxic. Dr. Key obtained approximately 57 per cent toxic reactions. European workers report from 40 to 50 per cent of toxic reactions, but we had only 17 per cent of toxic reactions in our clinic, and I myself have had no toxic reactions in my private cases. While Dr. Key followed the European advice with regard to giving not over 100 mg. of gold salts at any single injection, he appears to have exceeded the limit of what is usually considered a safe total dosage in any single series. In some cases he gave as high as 2, 4 and even 6 Gm. total dose to each patient. Differences of opinion exist as to what should constitute the total dose to be given in any one course of treatment. Hartfall and Garland say 1 Gm., Slot 1.2 Gm., Buckley from 1 to 1.5 Gm., Phillips 1.5 Gm., Williams from 1.8 to 2.4 Gm., Baker 2 Gm., Bach 2.5 Gm. It is obvious therefore that at the present time it is not as a general rule considered safe to give more than 1 Gm. in any single series, making a total of 3 Gm. for three series.

One cannot emphasize too strongly the point that, although gold is a valuable drug, it is also a dangerous one. The French and English rheumatologists believe gold salts to be the best single agent for the treatment of arthritis. While in this country medical opinion was hostile to this form of treatment until three years ago, I think the general attitude of the profession has been rapidly changing since then. I still cannot concede that it is the best single remedy for arthritis and I do not feel that it is advisable to use this drug in early cases that can be treated by safer methods. Toxic reactions, while usually preceded by pruritus, may appear suddenly and unsuspectedly, and for this reason constant vigilance is the price of safety when one is using this form of therapy. A severe toxic reaction may come on after a small initial dose or it may appear at any time during any series of treatments, even if there had been no symptoms of toxicity during the previous series. Occasionally one encounters a delayed toxic reaction, which may come on from one to three months after the last dose of gold salts. In my own experience the toxic reactions consisted largely of mild dermatologic reactions and gastrointestinal disturbances lasting from a week to ten days. In two cases, however, the reactions were severe. One patient had a dermatitis which lasted two and a half months. The other patient had an edema which involved the glottis and required a tracheotomy. Both patients received an initial dose of 10 mg. of sodium gold thiosulfate, followed in the first case by a second dose of 10 mg. and in the second case by a dose of 20 mg. Both patients made excellent clinical recoveries.

Gold salts have been used for the past ten years in Europe. During the first five years of their use a great deal of experimentation had to be done with regard to dosage and many fatalities resulted. Until three years ago the mortality rate in Europe was 3 per cent, but at the present time it is approximately 1 per cent. Dr. Key reports no fatalities in his series of seventy cases. We reported a series of 100 cases last year without any fatalities, but in spite of increasing experience, we have since had one death which resulted from aplastic anemia. We now question each patient carefully as to any unusual symptoms and also do a urinalysis as a matter of routine before each treatment with gold salts. In addition, we insist on a complete blood count at least once a month during the period of therapy. The exact way in which gold salts act is not known. In all probability the beneficial results observed are due in part to shock therapy, because many patients who have been given large doses develop typical chills and fever similar to those observed following the use of a foreign protein. It is interesting to note that Ken Yanagisawa and Sakae Kawai, two Japanese workers, have just pointed out that the only gold compounds therapeutically active are those which contain sulfur and in the treatment of experimental tuberculosis in guinea pigs they found that one of the compounds was just as effective when the gold was removed and the sulfur left in. In light of our recent experience, however, that it requires large doses of sulfur to produce beneficial therapeutic results in the treatment

of arthritis, the possibility that the beneficial results observed in gold therapy are due to the sulfur content seems rather remote. I should like to ask Dr. Key to express his opinion on this subject. I heartily agree with Dr. Key that every effort should be made to find a gold preparation which would be less toxic, although just as efficient as myochrysine.

DR. J. ALBERT KEY, St. Louis: Our first severe reaction was in a patient with spondylitis and that patient was in the hospital for about six weeks with exfoliative dermatitis, which was followed by furuncles. When he got out he wanted to have more gold treatments. The question of dosage is not settled. We have used the dose which is usually recommended and all our patients have had the same dose unless they were found to be sensitive and then we decreased it to a point of toleration. Our laboratory examinations were done about once a month. It would be better to do them more frequently. It isn't entirely luck that has prevented us from having deaths: part of it has been due to the fact that we have observed our cases and at the first sign of reaction we have stopped the treatment or diminished the dose. Observation must continue just as long as gold is given. Most of the reactions occur in the beginning, but they may occur in patients who have had as much as 2 Gm. of gold salt. We have had them, and quite severe ones.

#### Hydrotherapy in Osteo-Arthritis

DR. JOHN D. CURRENCE, New York: In osteo-arthritis there are certain accepted predisposing and exciting factors, although their relative importance may not be agreed on. These factors result in variable degrees of physiologic disturbances. It is only by the alleviation of this physiologic imbalance that symptomatic relief can be expected. My conclusions are drawn from the use of hydrotherapy in the treatment of more than 500 cases of osteo-arthritis seen during the past eight years. The recent observations are based on the treatment of 125 cases treated since the development of the technic described.

The physiologic reactions accomplished through the medium of water are accomplished:

1. Through the sensory stimulus to the nerves and resultant reflex.
2. By the warming or cooling action of the body, (a) by direct influence on the metabolic equilibrium, (b) by adding to or subtracting from the body heat.

The reciprocal reactions of the peripheral and splanchnic vascular beds are well known. Increased external temperature brings about a change in the blood volume ratio in favor of the peripheral structures. Actually, however, there is a reduction in the volume of the blood plasma.

The use of hydrotherapy in osteo-arthritis provides an extremely valuable adjunct to medical and orthopedic management of these cases. Judiciously planned courses of treatment, individualized to meet the specific requirements of the patient, are valuable not only in improving or restoring function but also in combating the predisposing and exciting factors of the disease. Although many patients may be benefited in their homes by improvised application of the principles set forth, institutional care is necessary to achieve the optimal result.

#### DISCUSSION

DR. RALPH PEMBERTON, Philadelphia: In general I can only approve the broad point of view Dr. Currence maintains toward hypertrophic arthritis (osteo-arthritis). I agree with him in his implications that the syndrome cannot be wholly accounted for by age and trauma alone. The intelligent use of suitable measures including physical therapy often illustrates this, since these patients may grow much older and successfully assume their subjective discomfort. There is one point in Dr. Currence's paper on which I must differ, viz. the recommendation that codeine be given to control pain. In my clinic we rarely give anodynes of any sort as they are not often needed, and codeine and morphine are never resorted to. As a matter of fact many patients when first seen have been taking acetylsalicylic acid, sometimes in large doses, and in the great majority of cases it is possible to reduce and omit it entirely within a week. I believe that any considerable use of anodynes in arthritis usually reflects unfamiliarity with the syndrome as a whole.

## Current Medical Literature

### AMERICAN

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Titles marked with an asterisk (\*) are abstracted below.

#### American J. Obstetrics and Gynecology, St. Louis

36: 545-726 (Oct.) 1938. Partial Index

Carcinoma of the Cervix: Consideration of Certain Problems Associated with Its Control. N. F. Miller and C. E. Folsome, Ann Arbor, Mich.—p. 545.

Relation of Pituitary Gland to the Menopause. B. P. Watson, P. E. Smith and R. Kurzrok, New York.—p. 562.

Relative Value of Pure Oxygen and of Carbon Dioxide Mixtures in Experimental Resuscitation. N. J. Eastman, Baltimore; R. B. Dunn, Greensboro, N. C., and J. Kreiselman, Washington, D. C.—p. 571.

\*Placental Transmission of Neorsphenamine in Relation to Stage of Pregnancy, with Special Reference to Prenatal Treatment of Syphilis. F. F. Snyder and H. Speert, Baltimore.—p. 579.

The Diet of the Pregnant Woman. E. V. McCollum, Baltimore.—p. 586.

Rhythmic Changes in the Skin Capillaries and Their Relation to Menstruation. J. I. Brewer, Chicago.—p. 597.

\*Geographic Distribution and Effect of Climate on Eclampsia, Toxemia of Pregnancy, Hyperemesis Gravidarum and Abruptio Placentae. W. J. Dieckmann, Chicago.—p. 623.

A Ten Year Study of Cesarean Section in the St. Louis Maternity Hospital. S. D. Soule, St. Louis.—p. 648.

Comparison of End Results of Treatment of Endocervicitis by Electro-physical Methods: Cautery, Coagulation and Conization. A. Jacoby, New York.—p. 656.

Effect of Sodium Lactate in Raising the Carbon Dioxide Combining Power in Toxemias of Pregnancy. L. C. Chesley and F. H. Vann, Jersey City, N. J.—p. 660.

Treatment of Late Abdominal Pregnancy: Report of Two Cases. A. C. Posner, New York.—p. 693.

**Placental Transmission of Neorsphenamine.**—In an attempt to measure the capacity of the placenta to transmit substances from the mother to the fetus, Snyder and Speert gave single injections of neorsphenamine to rabbits at various stages of pregnancy. In twenty-four fetuses obtained from twelve litters which were killed at various stages of pregnancy, there were striking differences in the quantities of arsenic recovered from the fetuses on examination one hour after the injection of arsphenamine. The arsenic content per fetus varied from none to 8 micromilligrams. When the stage of pregnancy was taken into consideration, it was evident that a definite correlation existed between the age of the fetus and its arsenic content. At twenty-five days no arsenic could be detected in the fetus. At twenty-seven days a small amount, estimated to be 0.25 micromilligram was found. From the beginning of the period of viability (twenty-eight days), increasingly larger amounts of arsenic were found in the fetus as pregnancy progressed; the greatest amount, 8 micromilligrams, was recovered at thirty-four days, or two days past term. In a second series of fourteen fetuses obtained from five litters in which twenty-four hours elapsed following injection the amount of arsenic in the fetus increased as term was approached. Arsenic was found in the fetus as early as the beginning of the latter half of pregnancy. The fetal portion of the placenta contained six times as much arsenic as did the maternal portion; the concentration of arsenic was only twice as great in the fetal as in the maternal portion. Gradual liberation of arsenic from the placenta to the fetus is indicated by the consistent finding of a greater amount of arsenic in the fetus twenty-four hours after injection than after one hour. The concentration of arsenic in the fetus near term approaches the level calculated to be present in the maternal tissues when definite antisyphilitic effect is exerted.

**Climate and Eclampsia.**—Dieckmann collected data as to the occurrence of eclampsia, nonconvulsive toxemia, hyperemesis gravidarum and abruptio placentae from various parts of the world. The meteorologic data have also been obtained for the various cities. Eclampsia, because of its striking symptoms and

signs, has been used as the index. Collected data show that the incidence ranges from 0 in many cities to 2.85 per cent in Algiers, Africa, and 7.2 per cent in Charlotte, N. C. The mean incidence for the world is 1 per cent, for the United States 0.66 per cent, for the British Isles 1.13 per cent, for Europe 0.68 per cent and for the rest of the world 0.52 per cent. There is some correlation, especially for the United States, between eclampsia, a high average temperature, a small range of temperature and a high measure of rainfall. The data seem to indicate that eclampsia may and undoubtedly does occur in the native who has had little or no contact with modern civilization. However, the latter with its mental strain and stress and change in diet and habits seems to cause an increase in the occurrence of eclampsia. The results warrant further investigation of the geographic distribution of these diseases as a means of determining pertinent factors, eliminating or preventing them and determining their relation to the etiology of the disease in question.

#### American Journal of Ophthalmology, St. Louis

21: 1083-1202 (Oct.) 1938

Nature of Ocular Fluids: II. Hexosamine Content. K. Meyer, Elizabeth M. Smyth and E. Gallardo, New York.—p. 1083.

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Glaucoma: Classification, Causes and Surgical Control: Results of Microgonioscopic Research. O. Barkan, San Francisco.—p. 1099.

Kayser-Fleischer Ring—Wilson's Disease. L. J. Goldbach, Baltimore.—p. 1118.

Lectures on Motor Anomalies: II. Theory of Heterophoria. A. Bierschowsky, Hanover, N. H.—p. 1129.

Studies on Inclusion Blennorrhoea: II. Expressional Transmission. L. A. Julienne, R. W. Harrison and A. C. Lange, St. Louis.—p. 1137.

Value of Routine in Examinations of the Eye. T. D. Allen, Chicago.—p. 1147.

\*Acute Epidemic Superficial Punctate Keratitis. L. C. Hobson, San Fernando, Calif.—p. 1153.

**Superficial Punctate Keratitis.**—The epidemic of keratitis that Hobson describes occurred at the Veterans Administration, San Fernando, Calif., during September and October 1936. Many of the characteristics of the keratitis checked with those reported by other observers. Clinically, in the sixteen cases a violent conjunctivitis (unilateral in only one) occurred; both ocular and palpebral conjunctivae were markedly reddened, swollen and edematous, with about equal severity in each eye, in contrast to the later corneal symptoms which affected one eye to a greater degree than the other. Photophobia and lacrimation were pronounced. Pain was not severe in the conjunctival stage, which lasted from ten to fourteen days and ran a rather definite course. Repeated smears and cultures made from material taken from conjunctival culdesacs of all patients failed to reveal the presence of offending organisms. The corneal lesions consisted of minute, opaque, grayish dots (from twenty to 100), involving, for the most part, the second layer of the cornea. Some may have extended into the deeper structures. The remedies usually employed in the conjunctival stage were more or less ineffectual. Keeping the patient in a dark room proved most beneficial. Either hot or cold compresses brought some relief. When pain was unbearable the instillation of pontocaine solution or ointment was recommended.

#### American Journal of Orthopsychiatry, Menasha, Wis.

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Therapeutic Effects of a Play Group for Preschool Children. Susan Burlingham, Philadelphia.—p. 627.

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Use of Authoritative Approach in Social Case Work in the Field of Delinquency. J. Slawson, New York.—p. 673.

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Deficiency in the Finger Schema in Relation to Arithmetic Disability (Finger Agnosia and Acalculia). A. Strauss and H. Werner, Northville, Mich.—p. 719.

Interrelated Factors in Development: Study of Pregnancy, Labor, Delivery, Lying-In Period and Childhood. Margaret E. Fries and Beatrice Lewi, New York.—p. 726.

## American Journal of Physiology, Baltimore

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- Relative Influence of Radiation and Convection on Temperature Regulation of Clothed Body. C. E. A. Winslow, L. P. Herrington and A. P. Gagge, New Haven, Conn.—p. 51.
- Effects of Ingestion of Glucose and of Fructose on Rate of Excretion of Urine and Various Constituents. G. Bachmann, J. Haldi, C. Ensor and W. Wynn, Emory University, Ga.—p. 77.
- Effect of Cocaine and of Ergotamine on Action of Renal Pressor Substance. J. R. Williams Jr., Nashville, Tenn.—p. 83.
- Effect of Acute Hemorrhage on Absorption from Small Intestine. E. J. Van Liere, D. W. Northup and C. K. Sleeth, Morgantown, W. Va.—p. 102.
- Organ Hypertrophy Following Injections of Thyrotropic Hormone. Rosemary Murphy, Stephanie Lowther and Lucia Pagniello, Wellesley, Mass.—p. 110.
- Relation of Estrogenic Substances to Thyroid Function and Respiratory Metabolism. T. C. Sherwood, Lexington, Ky.—p. 114.
- Concerning the Metabolism of Fat and Carbohydrate. J. L. Donnelly, Fort Thomas, Ky.—p. 126.
- Antagonism Between Posterior Pituitary Secretion and Acetylcholine. H. Necheles and F. Neuwelt, Chicago.—p. 142.
- Action of Excess Sodium, Calcium and Potassium on Coronary Vessels. L. N. Katz and E. Lindner, Chicago.—p. 155.
- Changes in Skin Temperatures of Extremities Produced by Changes in Posture. Grace M. Roth, M. M. D. Williams and C. Sheard, Rochester, Minn.—p. 161.
- Insulin Convulsions After Removal of Stellate Ganglia. R. A. Phillips and S. B. Barker, New York.—p. 202.
- Respiratory Exchange During High Carbohydrate Ingestion. J. H. Talbott, F. S. Coombs, W. V. Consolazio and L. J. Pecora, Boston.—p. 246.
- Chemical Mediators in Aqueous Humor. J. V. Lucco and K. Lissák, Boston.—p. 271.

## Am. J. Roentgenol. &amp; Rad. Therapy, Springfield, Ill.

40: 485-644 (Oct.) 1938. Partial Index

- Seventeen Years' Experience in Radiation Therapy of Cancer, Zurich, 1919-1935. H. R. Schinz, Zurich, Switzerland.—p. 485.
- Cancer of the Larynx: Results of Roentgen Therapy After Five and Ten Years of Control. H. Coutard, Chicago.—p. 509.
- \*Radiation Therapy of Chronic Mastitis. H. C. Taylor Jr. and R. L. Brown, New York.—p. 517.
- Osteoradionecrosis in Intra-Oral Cancer. W. L. Watson and J. E. Scarborough, New York.—p. 524.
- Radium Therapy in Primary Carcinoma of Urethra. I. I. Kaplan, New York.—p. 535.
- Roentgenologic Localization of Tumors Affecting Spinal Cord. J. D. Camp, Rochester, Minn.—p. 540.
- Tumors of Hypophysis Cerebri from a Roentgenologic Point of View. C. W. Schwartz, New York.—p. 548.
- Epiphyseolysis or Separation of Capital Epiphysis of the Femur in Adolescence. M. M. Pomeranz, New York.—p. 580.
- Significance of Lateral View of the Rectum: Description of Technique and Its Value. S. A. Robins and W. S. Altman, Boston.—p. 598.
- \*Subarachnoid Alcohol Injection for Relief of Brachial Neuritis: Use of Lipiodol Preliminary to High Spinal Alcohol Injection. H. C. Saltzstein and F. Schreiber, Detroit.—p. 606.

**Radiation Therapy of Chronic Mastitis.**—Taylor and Brown divide chronic mastitis into categories: circumscribed masses which require surgical excision and mild cases of mastitis in which no active treatment should be administered. Support of the breast, encouragement and reassurance, and the elimination of fatigue and worry will usually serve to reduce the symptoms of mild mastitis. There remains a small group of cases with diffuse disease of the breast and symptoms so severe as to demand relief. If the patient is more than 40, if she has had a sterilizing pelvic operation or if there is no probability of the patient's desiring children, roentgen castration may be undertaken with the practical certainty that the symptoms will improve. If the patient desires it, a smaller dose to cause only temporary sterilization may be given. This will produce temporary relief and probably permanent improvement and the larger dose can be given later if desired. If the patient is younger and desirous of retaining her fertility and menstrual function, direct roentgen irradiation of the breast may be undertaken. Improvement probably will not be complete and some cutaneous pigmentation is to be expected.

**Injection of Alcohol for Brachial Neuritis.**—Rather than the risks of high chordotomy or the drawbacks of chronic morphinism, Saltzstein and Schreiber think that the subarachnoid

injection of alcohol for the relief of brachial neuritis may be the method of choice in debilitated persons in whom life expectancy is uncertain and the safety of major operation doubtful. The patient is placed on a tilt table. The site of injection is arched with a pillow, the patient is pushed somewhat ventrad as for spinal injections of alcohol, and the needle is introduced at the desired level. Under roentgenoscopic control, one drop of ascending iodized oil is injected. The position of the iodized oil is ascertained. If it is not lying in the region of the roots of the nerve which it is desired to bathe, the table is tilted either up or down until it is exactly in the right place. Two cases are reported to illustrate the usefulness of the injection of iodized oil preliminary to high intraspinal injections of alcohol and to show the consequent relief obtained.

## Annals of Internal Medicine, Lancaster, Pa.

12: 429-576 (Oct.) 1938

- Nutritional Deficiency. G. R. Minot, Boston.—p. 429.
- \*Studies on Pathologic Physiology of the Exophthalmos of Graves' Disease. D. Marine, New York.—p. 443.
- Physiologic Methods in Diagnosis and Treatment of Asthma and Emphysema. A. L. Barach, New York.—p. 454.
- \*Pressor Reaction Produced by Inhalation of Carbon Dioxide: Studies of Patients with Normal Blood Pressure and with Hypertension. M. Hardgrove, Grace M. Roth and G. E. Brown, Rochester, Minn.—p. 482.
- Constitutional Reactions from Bacterial Vaccines. G. T. Brown, Washington, D. C.—p. 493.
- \*Skin Testing for Brucellosis (Undulant Fever) in School Children. F. E. Angle, W. H. Algie, Kansas City, Kan.; Leona Baumgartner, Washington, D. C., and W. F. Lunsford, Kansas City, Kan.—p. 495.
- Syphilis and Gonorrhea as Public Health Problems. J. L. Rice, New York.—p. 503.
- Systemic Reaction to Oral Fusospirochetosis Without Local Lesions. W. H. Barrow, San Diego, Calif.—p. 508.
- Cevitamic Acid (Ascorbic Acid, Crystalline Vitamin C), Critical Analysis of Its Use in Clinical Medicine. I. S. Wright, New York.—p. 516.
- Clinical and Hematologic Review of Sprue Based on Study of 150 Cases. R. M. Suarez, San Juan, Puerto Rico.—p. 529.
- The Social Responsibilities of Medicine. J. P. Peters, New Haven, Conn.—p. 536.

**Pathologic Physiology of Exophthalmos.**—Marine believes that thyroid insufficiency (relative or absolute) and anterior pituitary hyperactivity appear to be two of the essential factors underlying the development of the exophthalmos of toxic goiter. Yet the fact that exophthalmos does not occur in myxedema and cretinism clearly indicates that other factors than thyroid insufficiency and pituitary hyperactivity are necessary. Evidence has been reported indicating a definite sex difference in the incidence of thyroidectomy exophthalmos in both man and rabbits and that an increase in the functional activity of the interstitial cells and possibly of the adrenal cortex is necessary. Thyroidectomy with its ensuing increase in the activity of the sex gland, mediated both as a direct gonad-thyroid interrelationship and as an indirect one through the pituitary, and also the parenteral administration of synthetic androgens promote the development of exophthalmos in the rabbit. Gonadectomy abolishes and cryptorchidism maintains an existing exophthalmos in the rabbit. Disturbances in calcium and phosphorus metabolism (especially high phosphorus and low calcium) affecting neuromuscular irritability appear to be necessary additional factors.

**Pressor Reaction from Inhalation of Carbon Dioxide.**—Hardgrove and his colleagues determined the pressor reactions of twenty-one normal and forty-one hypertensive persons following the inhalation of 10 per cent carbon dioxide and 90 per cent oxygen and compared these responses with those which occur as a result of the cold test. The inhalation of carbon dioxide produced an increase in the blood pressure of normal and hypertensive persons. There was no qualitative difference in the vasopressor response of normal and hypertensive persons but a significant quantitative pressor reaction was obtained when cold was applied during the inhalation of the carbon dioxide and oxygen. When the cases of hypertension were divided into those in which the hypertension was in the early or preorganic stage and those in which the hypertension was in the advanced stage it was found that the increases which were produced in the blood pressure by the application of cold were greater in cases of early or preorganic hypertension than they were in cases of advanced hypertension. This was particularly true when cold was applied during the inhalation of carbon dioxide and oxygen. The basal blood pressure was lower in cases of preorganic

hypertension than it was in cases of advanced hypertension. The average increases in the blood pressures of normal and hypertensive persons were greater when cold was applied during the inhalation of carbon dioxide and oxygen than they were when cold was not applied during the inhalation. Since carbon dioxide has a specific stimulating effect on the vasomotor centers, the definite increase in blood pressure which occurs during the inhalation of carbon dioxide and oxygen may be assumed to indicate some hypersensitivity of the vasomotor centers. When cold was applied during the inhalation of carbon dioxide and oxygen a further increase took place. This might have been caused by a reflex transmission of peripheral stimulation to a higher reactive central mechanism that was still further sensitized by the increased concentration of carbon dioxide in the blood, but the response was most likely the result of several stimuli. These observations demonstrate that a stimulus applied to the periphery (local application of cold) or applied centrally by increasing the carbon dioxide concentration in the blood increased the blood pressure of normal and hypertensive persons. They throw no light on the question as to why the hypertensive person responds to a greater extent than does the normal person.

**Cutaneous Testing for Brucellosis.**—Simultaneous intradermal tests on 163 adults with vaccine and brucellergin indicated that heat-killed vaccine produces more severe reactions than brucellergin. In the thirteen cases that reacted most severely investigated by Angle and his associates, cutaneous testing was followed by a rise in titer of specific agglutinins. Positive reactions were obtained in 9 per cent of 7,122 school children by intradermal tests with brucellergin. There was an increasing percentage of positive cutaneous reactors in successive age groups up to early adulthood. Differences in reactions of males and females were found only in the 15 to 19 year old group and then only in white children. The lowest percentage of positive reactions was found in Negro children. Of the positive reactors 79.3 per cent consumed raw milk. There was no correlation between positive brucellergin and positive tuberculin reactions.

### Archives of Dermatology and Syphilology, Chicago

38: 679-836 (Nov.) 1938

- Urticaria Provoked by Heat or by Psychic Stimuli. J. G. Hopkins, B. M. Kesten and O. G. Hazel, New York.—p. 679.  
Tabes Dorsalis: Cooperative Clinical Studies in Treatment of Syphilis. P. A. O'Leary, Rochester, Minn.; H. N. Cole, Cleveland; J. E. Moore, Baltimore; J. H. Stokes, Philadelphia; U. J. Wile, Ann Arbor, Mich.; T. Parran, R. A. Vonderlehr and Lida J. Usilton, Washington, D. C.—p. 692.  
\*Lymphogranuloma Venereum, Especially Its Treatment with Sulfanilamide. L. W. Shaffer and Effie Arnold, Detroit.—p. 705.  
The Trichophylin Test: Its Value as a Diagnostic Aid. G. M. Lewis, G. M. MacKee and Mary E. Hopper, New York.—p. 713.  
Significance of Porphyrin Content of Urine in Dermatoses Associated with Sensitivity to Light. A. R. McFarland and W. H. Strain, Rochester, N. Y.—p. 727.  
\*Diagnostic and Therapeutic Use of Tuberculin in Certain Acneform Eruptions. M. T. Van Studdiford, New Orleans.—p. 737.  
Contact Dermatitis from "Horn-Rimmed" Spectacles: Report of Case. H. S. Berkoff, New York.—p. 746.  
Prognostic Significance of Cutaneous Lesions in Coccidioid Granuloma. E. Epstein, Oakland, Calif.—p. 752.  
Sycosis Parasitica Due to Favotrichophyton Album Var. Singulare. J. A. Gammel and J. L. Work, Cleveland.—p. 756.  
Susceptibility of Allergic and Nonallergic Persons to Rhus Toxicodendron. F. C. Knowles, H. B. Decker, A. G. Pratt and J. A. Clarke Jr., Philadelphia.—p. 773.

**Venereal Lymphogranuloma.**—Shaffer and Arnold present a study of forty-six Negro women with venereal lymphogranuloma, including observations on their treatment. In cases of late involvement in which vulvovaginal ulcers are present, after some healing and elephantiasis occur, characteristic polypoid masses develop about the entrance to the vagina and around the rectum. The average age of the patients was 29 years. The commonly accepted methods of treating the disease were entirely unsatisfactory. With the introduction of sulfanilamide and its use in greatly diversified infections, it was used in this infection in twenty-two cases. The drug was given entirely by mouth, 40 grains (2.6 Gm.) daily in four doses of 10 grains (0.65 Gm.) each for one week; 30 grains (2 Gm.) daily in three doses of 10 grains each for the second week, and 20 grains (1.3 Gm.) daily in four doses of 5 grains (0.3 Gm.) each for the remainder of the time. The usual length of treatment was from one or two months. The results with such small doses have been

encouraging. Of the twelve cases in which sulfanilamide alone was used, apparent cure occurred in three, improvement in five and no improvement in two; the results in two are unknown. Of the ten cases in which there had been previous treatment (usually intradermal injections of Frei antigen, administration of antimony and potassium tartrate, treatment for coexisting syphilis or a combination of these, none of which produced material benefit), seeming cure occurred in one, improvement in six and no improvement in one; the results are unknown in two. The rapid symptomatic improvement in the majority of cases, even of severe chronic involvement, is gratifying. Longer observation will be necessary to determine the permanence of these results. The seemingly specific results may be due to action of the drug on the secondary invaders rather than on the specific virus of the disease. Sulfanilamide may be an effective weapon also in the prophylaxis of venereal lymphogranuloma.

**Tuberculin in Acneform Eruptions.**—Because certain acneform eruptions did not respond to the usual methods of treatment, Van Studdiford performed tests with old tuberculin in forty-nine of 111 cases and followed these tests with the administration of tuberculin as a therapeutic measure. Later, routine tuberculin tests were made on all patients with cystic acne who were free of pyogenic infections or menstrual disturbances. As diagnostic agents human bovine and old tuberculin were injected intradermally in each forearm, 0.1 mg. of 1:100,000, 1:10,000 and 1:1,000 dilutions being used, and a reading was made in forty-eight hours. Therapeutic injections were made into the deltoid muscle; the starting dose was 0.1 mg. of a 1:100,000 dilution. This dose was repeated and doubled every other five to seven days until 0.4 mg. of a 1:100,000 dilution had been given for two doses and a total of six doses given. Then 0.1 mg. of a 1:10,000 dilution was given by the same method until six doses had been given, after which doses of from 0.1 to 0.4 mg. of a 1:1,000 dilution were given weekly over a period of months. Some of the patients in the series have continued the injections for six months, after which a rest period was observed. Others stopped treatment after the cutaneous lesions cleared. Some of those who stopped treatment have had a recurrence of the lesions and have commenced receiving the injections again. All patients were given calcium, creosote and cod liver oil capsules as a routine tonic. Of twenty-five patients treated for sixty days or more with old tuberculin, ten were well and eleven improved; four are not included in the series because of the short time they have been under treatment. Tuberculin gives good results in the treatment of tuberculoderma; used with care it has cleared up long-existing acneform lesions and has caused no untoward effects.

### Archives of Otolaryngology, Chicago

28: 497-662 (Oct.) 1938

- \*Suppuration of Petrous Pyramid: When and How to Operate: Report of Thirty Cases. R. L. Moorhead and J. P. Baker, Brooklyn.—p. 497.  
Scleroma (Rhinoscleroma): Report of Three Cases. L. F. Morrison, San Francisco.—p. 531.  
Complications Following Rhinoplasty. A. Palmer, New York.—p. 538.  
Orogenic Aspects of Arachnoiditis. S. L. Shapiro, Chicago.—p. 546.  
The Nasogenital Relationship. S. Rosen, New York.—p. 556.  
Morphologic and Roentgenologic Aspects of Temporal Bone: Study of 536 Bones, with Special Reference to Pneumatization. C. C. R. Jackson, Cleveland.—p. 561.  
Psychology of Laryngectomized Patients. L. A. Schall, Boston.—p. 581.  
Indications for Different Types of Treatment of Malignant Disease of the Larynx. C. J. Imperatori, New York.—p. 585.  
\*Meningitis from the Sphenoid Sinus. R. W. Teed, Ann Arbor, Mich.—p. 589.  
Purulent Otitis Media, Sinus Thrombosis and Suppuration of Petrous Pyramid: Acute and Chronic Forms. S. J. Kopetzky, New York.—p. 626.

**Suppuration of Petrous Pyramid.**—Since the recognition and the treatment of petrosal suppuration have advanced and the mortality has been reduced to a low figure by the various types of operations, Moorhead and Baker believe that now the otologist should pay more attention to the hearing of the patient. A study of the postoperative audiograms of many of their patients shows that the preservation of hearing can be accomplished if the radical mastoid operation is avoided.

**Meningitis from the Sphenoid Sinus.**—Teed presents a historical review of the reported cases (129) of meningitis from the sphenoid sinus and gives abstracts of the reports of some of the first cases, most of which are not included in previous

monographs on the subject. Statistical reports are studied and the conclusion is drawn that while the sphenoid sinus is involved in about 15 per cent of clinical cases of sinusitis and in 33 per cent of pathologic cases it is nevertheless responsible for approximately 35 per cent of all rhinogenous intracranial complications. Evidence is presented which indicates that the spread to the meninges and venous spaces is predominantly vascular and that this extension is aided by the close anatomic relation of the vascular marrow spaces of the sphenoid bone with the infected mucosa of the sinus. The further relation between disease of the sphenoid sinus and of the pituitary body and insanity is observed, with evidence that, in certain cases of mental aberration, resolution of the infection within the sphenoid sinus is remedial. With the recent increase of interest in this subject and with the knowledge of the symptomatology and associated pathologic changes in disease of the sphenoid sinus, the author hopes that the next few years will show a decrease in the deaths from this cause, not so much from treatment but from prevention by early attack on the diseased sphenoid sinus.

### California and Western Medicine, San Francisco

49: 249-352 (Oct.) 1938

- Some Contributions by Animals to Human Health. A. C. Ivy, Chicago.—p. 257.  
Seven Wonders of Medical Science—Modern Miracles. A. C. Ivy, Chicago.—p. 260.  
Antivivisection. C. Rowell, Berkeley.—p. 263.  
Subcutaneous Emphysema with Asthma. H. D. Van Fleet, H. Miller and A. J. Scott, Los Angeles.—p. 265.  
Obstetric Observations: Some Ideas and Procedures Not Commonly Found in the Textbooks. B. Bakewell, Santa Barbara.—p. 268.  
\*Adrenal Cortex in Treating Childhood Asthma: Clinical Evaluation of Its Use. F. M. Pottenger Jr. and F. M. Pottenger, Monrovia.—p. 271.  
Dynamic Approach to Pulmonary Tuberculosis. H. G. Trimble, Oakland, and B. H. Wardrip, San Jose.—p. 276.  
Gastric Ulcer: Indications for Medical and Surgical Treatment. W. C. Boeck, Los Angeles.—p. 281.  
Water Exchange in Surgical Cases. D. A. Charnock, Los Angeles.—p. 287.  
Specific Sensitization in Nonspecific Urethritis. J. Steinberg, Los Angeles.—p. 291.  
Aleukemic Myelosis (Aleukemic Leukemia), with Special Reference to Clinical Significance of Myeloblast: Analysis of Twenty Cases. S. R. Mettler and Katherine Purviance, San Francisco.—p. 296.  
Social Security: In Relation to the Physician. W. B. Dakin, Los Angeles.—p. 300.

**Adrenal Cortex in Childhood Asthma.**—The Pottengers analyze a group of fifty allergic crippled patients complaining of asthma who have been under treatment for one year or longer. The whole adrenal gland has been found more effective than epinephrine alone, and most effective when given with a high salt intake. The authors now utilize a semiketogenic diet which, on the basis of an adult diet, consists of approximately 2,300 calories, roughly 145 Gm. of fat, 145 Gm. of protein and 100 Gm. of carbohydrate. It is rich in known vitamins and minerals. The two main meals are built around a large, raw salad and a portion of meat consisting of not less than 4 ounces when cooked. Sugar and all foods high in carbohydrates except whole grain, fresh ground cereals, are largely eliminated. Gelatin is used, one-half ounce or more at each meal, because of its hydrophilic colloidal properties, which aid in digestion and mineral assimilation. The vitamins, other than those contained in the large green salad, are administered in the form of a high grade raw green pasture milk, malt and cod liver oil. The complete therapy used for any person depends on the results of the physical examination. Of the fifty patients treated, 84 per cent showed improvement in their allergic symptoms and physical improvement was observed in 90 per cent. Six of the thirty-five boys in the group presented nondescent of one or both testes, all six of which showed descent under treatment. Evidence of thyroid or genital disturbance was obtained in 74 per cent of the mothers of the patients. Forty of the fifty patients were taller than normal standards.

### Connecticut State Medical Society Journal, Hartford

2: 477-522 (Oct.) 1938

- The Traffic in Drugs. T. G. Klumpp, Washington, D. C.—p. 477.  
Syphilis and Psychiatry. E. Kahn, New Haven.—p. 481.  
Reeducation of the Problem Drinker. C. H. Durfee, Wakefield, R. I.—p. 486.  
Skin Tests in Allergy. F. M. Rackemann, Boston.—p. 495.  
Analysis of Obstetric Material at the Grace Hospital of New Haven. H. B. Perrins and M. L. Berlowe, New Haven.—p. 499.

### Johns Hopkins Hospital Bulletin, Baltimore

63: 209-282 (Oct.) 1938

- Human Elliptic Red Corpuscles. A. L. Florman and M. M. Wintrobe, Baltimore.—p. 209.  
Congenital Myotonia in Goats: Description of the Disease. Effect of Quinine, Various Cinchona Derivatives, Other Alkaloids and Salts on Myotonic Symptom. L. C. Kolb, Baltimore.—p. 221.  
\*Effect of Alcoholic Intoxication and Ether Anesthesia on Resistance to Pneumococcal Infection. K. L. Pickrell, Baltimore.—p. 238.  
Partial Atresia of the Main Branches of Pulmonary Artery Occurring in Infancy and Accompanied by Calcification of Pulmonary Artery and Aorta. Ella H. Oppenheimer, Baltimore.—p. 261.

**Intoxication and Resistance to Pneumococcal Infection.**—Pickrell carried out experiments on 175 rabbits in order to determine whether alcoholic intoxication lowers the resistance to pneumococcal infection and, if it does, to discover the mechanism by which it exerts its effect. Animals well immunized to type I pneumococci were used. The experiments make it clear that the loss of immunity during alcoholic intoxication or ether or tribromethanol anesthesia is not due to the fact that the leukocytes are paralyzed but rather to their failure to emigrate. The failure to emigrate appears to be due to an effect of intoxication or anesthesia on the vascular inflammatory mechanism. In the intoxicated body the capillaries fail to respond to the presence of an inflammatory irritant with dilatation and increase in their permeability. The failure of the capillaries to react to irritants in the usual manner in intoxicated animals is the only reason for the absence of leukocytic emigration that has been disclosed by the present studies. In what manner intoxication acts to prevent the usual inflammatory alterations in the capillaries is at present obscure, but that it does so is clearly evident. The experiments emphasize the essential role of the phagocyte in protection against pyogenic bacteria even when humoral immunity is present in high degree. Pneumococci proliferated to enormous numbers in the absence of leukocytes at the site. Agglutination of the bacteria in the tissues under the influence of the antibody was evident. Although abundant leukocytes were present in the blood stream, their failure to escape permitted the progressive growth of the bacteria even in the presence of abundant antibody. The studies demonstrate that if bacteria are aspirated into the lungs during deep intoxication or anesthesia they will grow uninhibited by the defenses of the body during the entire period of unconsciousness, and this, regardless of the amount of immunity possessed by the body against the bacteria. If the bacteria are able to grow unrestrictedly during several hours, they may easily become so numerous that inflammation developing after recovery of consciousness may be unable to overcome them.

### Journal of Immunology, Baltimore

35: 245-328 (Oct.) 1938

- Absorption of Pneumococcus Antibody After Intramuscular Injection of Antipneumococcus Horse and Rabbit Serums. M. Finland and J. W. Brown, Boston.—p. 245.  
Spread of Tubercle Bacilli in Bodies of Sensitized and Immunized Animals. J. Freund and D. M. Angevine, New York.—p. 271.  
Simplified Photomicrometric Technic for Titration of Antibody Potency of Antipneumococcus Horse and Rabbit Serum. R. L. Libby, Pearl River, N. Y.—p. 289.  
Ablastic and Trypanocidal Antibodies Against Trypanosoma Duttoni. W. H. Taliaferro, Chicago.—p. 303.

### Journal of Thoracic Surgery, St. Louis

8: 1-126 (Oct.) 1938

- Extrapleural Thoracoplasty in Presence of Contralateral Pneumothorax. E. J. O'Brien, W. M. Tuttle, J. C. Day, Detroit, and J. P. O'Connor, Pasadena, Calif.—p. 1.  
Giant Tuberculous Cavities of the Lung: Pathogenesis, Pathologic Physiology and Surgical Treatment. P. N. Coryllos and G. G. Ornstein, New York.—p. 10.  
Extrapleural Thoracoplasty: Further Experiences with Muscle Splitting Operation. J. R. Head, Chicago.—p. 55.  
Thoracoplasty for Tuberculosis and Chronic Empyema Through Short Incisions: Experiences with a New Method of Rib Removal, Including Description of Anterior Extrascapular Apicolysis. O. H. Wangenstein, Minneapolis.—p. 60.  
\*Indications, Hazards and Results of Apicolysis Thoracoplasty. J. W. Gale and W. H. Oatway Jr., Madison, Wis.—p. 78.  
Myoplastic Thoracoplasty. E. F. Butler, A. M. Skinner, Oneonta, N. Y.; R. Douglass, Ithaca, N. Y., and C. G. Merkel, Mount Morris, N. Y.—p. 93.

**Apicolysis Thoracoplasty.**—The ideal indications for apicolysis thoracoplasty that Gale and Oatway list are a relatively good condition and clinical inactivity of the patient, a normal, a stable, or a controlled contralateral lesion, absence of severe

tuberculous or nontuberculous extrapulmonary complications, functional need for selective partial collapse therapy, thin-walled cavitative lesions of considerable size or extent, single or multiple cavities in the upper paravertebral region and bilateral apical disease which makes a bilateral partial collapse necessary. The contraindications include relatively poor condition and clinical activity of the patient, an active, an unstable or an uncontrolled contralateral lesion, presence of severe tuberculous or nontuberculous extrapulmonary complications, large thick-walled cavitative lesions, gross apicohilar fibrosis (which if displaced caudally in its entirety might cause obstruction of larger bronchi or great vessels or later require otherwise unnecessary operations to obtain satisfactory collapse), large thick-walled cavities, dense peripleural fibrosis which prevents a safe dissection and small thin-walled cavitation occurring laterally. The authors have not found a progressive improvement in their statistical results. A fair comparison of apicolysis with the paravertebral operation cannot be made, since patients subjected to the latter had less destruction of the lungs and were better risks. The unfavorable results include the failure to close some thick-walled and certain check valve cavities. The sputum was converted in a high percentage of the cases, but more sensitive tests of the bronchial secretion were not as completely influenced. The immediate mortality was probably somewhat increased by the procedure. Atelectasis occurred and persisted too frequently but can be avoided by observing the predisposing factors, by careful individualization and by decreasing the size and extent of the lysis. It can be treated by taking immediate steps to evacuate and ventilate the obstructed portion of the bronchial tree. Scoliosis has not been avoided completely, but the localization of collapse has resulted in less incarceration of the scapula. The favorable results include a greater selectivity of collapse and conservation of functioning wall of the chest and pulmonary tissue. Collapses have been most perfect in lesions with the least fibrosis.

### Medicine, Baltimore

17:261-380 (Sept.) 1938

\*Rheumatic Subcutaneous Nodules and Simulating Lesions. H. Keil, New York.—p. 261.

**Rheumatic Subcutaneous Nodules and Simulating Lesions.**—From the data that Keil presents he believes that the following principles should be established: 1. The term rheumatic nodule should be applied to lesions occurring in the course of undoubted rheumatic fever. The highest degree of clinical specificity is observed in childhood, and the rheumatic subcutaneous nodule may be said to be highly specific of rheumatic fever in this age group. 2. The specificity of the rheumatic nodule is dependent on its clinical properties and relations. The combination of pathologic changes found in microscopic examinations, while often suggestive, shows no pathognomonic characteristics and may be simulated by other lesions. 3. The true rheumatic nodule is practically always associated with clinical evidence of cardiac involvement in one form or another. 4. The typical nodule in rheumatoid arthritis differs from that in rheumatic fever in many clinical attributes and in some pathologic respects. The clinical differences appear to be more important than the pathologic differences, the latter still requiring evaluation. 5. The nodule in rheumatoid arthritis shows greater resemblances to the juxta-articular node in syphilis. 6. The conception of the syphilitic nodule as an entity rests on three features: its association with other manifestations of syphilis, the almost invariable presence of a positive Wassermann reaction and the striking response to antisymphilitic therapy. 7. The controversy regarding the relative incidence of subcutaneous lesions in rheumatoid arthritis and in syphilis is clarified by the realization that both varieties of nodules occur but that their respective incidence will be governed largely by the type of material under observation. 8. The pathologic appearance of a rheumatic nodule, as observed in the ordinary microscopic examinations, is not pathognomonic of a single disease. How far the supravital studies will provide criteria for the differentiation of the various nodules is still problematic, but it is a method worthy of extended investigation. Caution is advised in drawing etiologic conclusions on the basis of morphologic resemblances.

### Mental Hygiene, New York

22:529-712 (Oct.) 1938

Mental Attitudes of Tuberculous Patients. E. A. Strecker, F. J. Braceland and B. Gordon, Philadelphia.—p. 529.  
Intelligence and Social Adjustment. Catharine Cox Miles, New Haven, Conn.—p. 544.  
Group-Clinic Approach to Delinquency. K. I. Wollan and G. E. Gardner, Boston.—p. 567.  
Group Autonomy in a Children's Institution. N. C. Kephart, Northville, Mich.—p. 585.  
Social Factors in the Case Histories of 100 Underprivileged Homosexuals. G. W. Henry and A. A. Gross, New York.—p. 591.  
Relationship Between Education and Mental Hygiene. E. V. Pullias, Los Angeles.—p. 612.  
Psychiatry and Protective Work. E. H. Adams, New York.—p. 625.  
Marriage Rates Among Patients with Mental Disease. B. Malzberg, Albany, N. Y.—p. 634.

### New England Journal of Medicine, Boston

219:547-590 (Oct. 13) 1938

The Diabetic Situation in Massachusetts. E. P. Joslin, Boston.—p. 547.  
Attitudes in Relation to Illness. L. K. Lunt, Concord, Mass.—p. 557.  
Sulfanilamide: Its Mode of Action and Use in Treatment of Various Infections. C. S. Keefer, Boston.—p. 562.  
Significance of Latent Forms of Tuberculosis. J. B. Amberson Jr., New York.—p. 572.

219:591-634 (Oct. 20) 1938

American Contributions to Nosography. D. Riesman, Philadelphia.—p. 591.  
Closed Intrapleural Pneumonolysis with One-Piece Operating Thoracoscope. L. Rabinowitz and E. J. Rogers, Pittsford, Vt.—p. 611.  
Physiologic Dulness of the Right Apex: Summary of Opinions. R. W. Buck, Boston.—p. 615.

### New York State Journal of Medicine, New York

38:1313-1368 (Oct. 15) 1938

\*Lead Poisoning: Newer Concepts in Treatment. I. Gray and I. Greenfield, Brooklyn.—p. 1313.  
Reorientation in the Public Health and Hospital Organization Patterns of Our Communal Life. E. H. L. Corwin, New York.—p. 1320.  
Activation of Disease by Trauma. J. J. Moorhead, New York.—p. 1327.  
Receding Chin: Plastic Reconstruction. J. Safian, New York.—p. 1331.  
Argyria Due to Silver Arsphenamine. O. Steinbrocker, New York.—p. 1335.  
The Hard of Hearing Patient and His Physician. J. W. Durkee, Morristown, N. J.—p. 1336.  
Adenocarcinoma of the Stomach, with Hemorrhagic Diathesis. C. E. McLeod and R. H. Goodale, Worcester, Mass.—p. 1339.  
Biliary Cirrhosis with Diabetes Mellitus Simulating Hemochromatosis: Report of Case. M. Campbell, S. S. Adler and J. F. Hart, New York.—p. 1342.

**Lead Poisoning.**—Gray and Greenfield cite two cases illustrating the dangers of deleading in acute lead poisoning and four cases illustrating the increased lead stream with a high calcium regimen. An adequate phosphorus intake is important for the formation of the insoluble dibasic lead phosphate which is stored in the skeletal system as the insoluble tertiary lead phosphate. Furthermore a large intake of phosphorus is necessary for normal bone metabolism and for the formation of an insoluble lead phosphate in the intestinal tract. The reabsorption of lead which may be excreted in the intestinal tract may be prevented if there is sufficient phosphorus in the diet. Under normal conditions the insoluble tertiary phosphate of lead is deposited in the bony tissues. Since this salt is retained as a skeletal deposit, the bones gradually remove lead from the circulating blood. The two processes of storage and excretion take place during the absorption of lead and continue after absorption has ceased, until practically all the lead in the body is held by the skeleton. While this state of affairs exists the stored lead is apparently harmless and symptoms of intoxication disappear. In isolated instances deleading may be helpful when the question of lead poisoning is considered in a differential diagnosis. The importance of deleading in the differential diagnosis is the finding in biologic materials of lead below that which may be considered normal. If after a period of deleading therapy (from seven to ten days) lead is found in quantities which fall within the range of normal limits it may be excluded as the agent responsible for the symptoms. The exception may be the individual who has had a short period of exposure to the absorption of lead. Deleading may be of value occasionally in continued litigation to determine whether an abnormal storage of lead exists and is responsible for the continued subjective symptoms in the absence of objective observations. If after deleading for a suitable period the amount of lead excreted in the biologic materials is within normal limits, the symptoms



may have been due to the toxic effects of the lead absorbed during a previous exposure and not to waves of liberation. In a case of acute lead intoxication, deleading therapy should not be attempted because of the danger of neurologic complications. When deleading is decided on, it is advisable to continue such treatment for no longer than seven or ten days. Occasionally there may be gastrointestinal disturbances associated with the administration of drugs and the acidosis produced during this form of therapy. A high calcium regimen is probably the best means of rapid deleading. The danger of neurologic complications during deleading, even among those in whom there is no acute lead intoxication, is a hazard which can be detected early only when the patient is under careful institutional observation.

### Psychiatric Quarterly, Utica, N. Y.

12: 613-820 (Oct.) 1938. Partial Index

- Psychiatric Classification in a Prison: Part I. Defects in the American Prison Association. A. N. Foxe, Comstock, N. Y.—p. 617.
- Acute Heterosexual Inadequacy: I. In the Male. Jane E. Oltman and S. Friedman, Concord, N. H.—p. 669.
- Prognostic Possibilities of the Rorschach Method in Insulin Treatment. Z. Piotrowski, New York.—p. 679.
- Neurologic Observations in Hypoglycemic States. P. Hoch, Ward's Island, N. Y.—p. 690.
- \*Occurrence of Relapses in Patients Treated with Insulin Hypoglycemic Shock. W. A. Horwitz, J. R. Blalock and M. M. Harris, New York.—p. 716.
- Electrocardiographic Studies of Patients Receiving Convulsant Doses of Metrazol in Treatment of Schizophrenia: Preliminary Report. Mildred Pellens, Wingdale, N. Y.—p. 722.
- Psychologic Performance Tests as Prognostic Agents for Efficacy of Insulin Therapy in Schizophrenia. M. Marjorie Bolles, G. P. Rosen and C. Landis, New York.—p. 733.
- \*Use of Intravenous Sodium Amytal in Psychogenic Amnesic States. M. Herman, New York.—p. 738.
- Testosterone in Male Involuntary Melancholia: Preliminary Report. H. S. Barahal, Kings Park, N. Y.—p. 743.
- Uronic Acids in Schizophrenia and Epilepsy: Preliminary Report. C. N. Baganz, Lyons, N. J.—p. 750.
- Control of Tuberculosis in the Hudson River State Hospital. A. A. Leonidoff, Poughkeepsie, N. Y.—p. 754.

**Relapses After Hypoglycemic Shock.**—Horwitz and his associates state that in sixty-seven psychotic patients treated with insulin there were thirty-one complete and social remissions (twenty recovered and eleven were much improved). Most of the patients who recovered were sick for less than one year. Eight relapses occurred in these thirty-one patients. Six of these were from the group of twenty considered recovered and two were from the group of eleven considered much improved. Of the fifteen women who recovered and the five who were much improved relapses occurred in seven. Two of the seven relapses occurred within a month after the patients left the hospital; the others occurred three, four, seven, ten and ten months, respectively. Of the eight patients in whom relapse occurred, two were retreated and again reached their maximal level of improvement (both of them have been on parole now for about seven months), four are still receiving their second course of treatment and again seem to be improving and two have shown no favorable response to the second course. No criteria are available as to the type of patient in whom relapse will occur.

**Sodium Amytal in Psychogenic Amnesia.**—Herman restored the memory of six persons with hysterical amnesia by giving sodium amytal intravenously. Their memory was restored within a few minutes. In each case other methods, including hypnosis, had been tried without success. Many theories have been evoked to explain the action of sodium amytal in producing its psychologic effect. The most likely theory is the physiologic explanation that sodium amytal is a cortical depressant and tends to diminish the normal inhibitory action of the cortical cells.

### Public Health Reports, Washington, D. C.

53: 1855-1906 (Oct. 21) 1938

- \*Studies on Immunizing Substances in Pneumococci: VII. Response in Human Beings to Antigenic Pneumococcus Polysaccharides, Types I and II. L. D. Felton.—p. 1855.
- \*Id.: VIII. Report on Field Tests to Determine Prophylactic Value of Pneumococcus Antigen. G. M. Ekwurzel, J. S. Simmons, L. I. Dublin and L. D. Felton.—p. 1877.

**Prophylactic Value of Pneumococcus Antigen.**—The present study by Felton and his associates is a continuation of the investigation of the activity of the antigenic polysaccharide of the pneumococcus in human beings and an analysis of the

prophylactic value of a pneumococcus antigen used in field tests on CCC volunteers. A test is described for white mice which apparently determines the presence of reacting substances and consequently may be used to assure an antigen suitable for injection without reactions in human beings. A type I antigen, shown to be specific for white mice, produced antibodies in children against type II of almost as high a titer as against type I organisms. Conversely, one preparation of specific type II antigen stimulated type I antibody in only one of five children tested. In adults the same specific antigens produced heterologous immunity. A test of thirty-five subjects one year after injection of 2 mg. of polyvalent antigen showed the presence of type I serum antibody in 51 per cent and of type II antibody in 77 per cent of the group. In all, 281 persons varying in age from birth to 79 years have been inoculated and tested for serum antibodies against type I and 276 against type II pneumococci. There was no transfer of the antibody to the baby from two mothers who had been immunized before delivery. All babies less than 1 year of age and six adults in the type I group and two in the type II series showed no antibodies either before or after the injection. All others, following a single injection of 2 mg. of antigen, showed an increase, although varying in amount, of serum antibodies against both type I and type II pneumococci. An analysis of the records of the present experiments suggests that this or a similar antigen may prove to be a useful tool for the control of the incidence of pneumonia, as in two groups of CCC camps, as compared with control groups, the incidence was reduced from 7.28 to 4.34 and from 15.69 to 1.73, respectively, per thousand years of life. The present experiments provide no indication as to the length of time for which the inoculations of antigen may influence the pneumonia morbidity rates. There is some indication that the antigen may be most effective for adolescents and that it loses its effectiveness with advancing age. There was no satisfactory evidence found to show that the antigen will lower the incidence of respiratory conditions other than pneumonia.

### Rhode Island Medical Journal, Providence

21: 141-158 (Oct.) 1938

- Sulfanilamide in Treatment of Beta Hemolytic Streptococcus Infection. K. K. Gregory, Providence.—p. 141.
- Sulfanilamide in Treatment of Other Bacterial Infections. R. E. Stevens, Providence.—p. 145.
- The Nasal Airways. J. R. Richardson, Boston.—p. 149.

### Yale Journal of Biology and Medicine, New Haven

11: 1-96 (Oct.) 1938

- Carcinogenic Chemical Agents. J. W. Cook, London, England.—p. 1.
- Recovery of Virus of Poliomyelitis from Extraneural Sources in Man, with a Survey of the Literature. A. J. Vignec, J. R. Paul and J. D. Trask, New Haven, Conn.—p. 15.
- Alkyl Sulfates: Their Selective Bacteriostatic Action. P. B. Cowles, New Haven, Conn.—p. 33.
- Local Increase of Pigmentation in Skin of CBA Mice by Application of Benzene. W. Bergmann, L. C. Strong and G. M. Smith, New Haven, Conn.—p. 39.
- Sacral Teratoma Complicating Labor. C. E. Tribble, De Land, Fla.—p. 45.
- \*Ulcers of the Digestive Tract in Association with Cerebral Lesions. L. Oppen and H. M. Zimmerman, New Haven, Conn.—p. 49.
- Fungus Infection of the Vagina: Case. L. Weinstein and R. M. Lewis, New Haven, Conn.—p. 85.

**Gastrointestinal Ulcers and Cerebral Lesions.**—Oppen and Zimmerman give the clinical histories and postmortem observations in twenty-two cases showing ulceration, erosion or malacia of the upper part of the digestive tract (esophagus, stomach or duodenum). Lesions of varied etiology were found in the brain of each of the twenty-one cases that came to necropsy. In one additional instance the brain was not examined but the clinical symptomatology pointed to organic cerebral involvement. These lesions were localized as follows: the nuclei of the interbrain in sixteen instances, the midbrain in two instances and diffuse cerebral, chiefly cortical, involvement in three instances. In the three latter cases the diencephalic nuclei were spared. The gastrointestinal lesions in cases of cortical and mesencephalic involvement are probably mediated through the hypothalamic nuclei. Two cases are described in which injury to the diencephalon and mesencephalon was not complicated by lesions in the digestive tract. Such instances emphasize the present lack of knowledge concerning the pathogenesis of lesions of the alimentary tract.

## FOREIGN

An asterisk (\*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

### British Journal of Anaesthesia, Manchester

16: 1-40 (Oct.) 1938

- Pentothal Acid: New Basal Anesthetic. J. S. Horsley.—p. 1.  
The Student Anesthetist. P. Ayre.—p. 10.  
Anesthesia and the Law. H. G. Dodd.—p. 16.  
Pregnancy: Contraindication to Spinal Analgesia. F. B. Mallinson.—p. 22.  
Anesthesia in Cardiac Surgery. J. K. Hasler.—p. 30.

### British Journal of Ophthalmology, London

22: 577-640 (Oct.) 1938

- Suppression of Vision in Squint and Its Association with Retinal Correspondence and Amblyopia. T. A. B. Travers.—p. 577.  
New Technic for Application of Radon Seeds to Sclera in Treatment of Glioma Retinae. H. B. Stallard.—p. 604.  
Cataract Associated with Hereditary Retinal Lesion in Rats. Margherita Cotonio Bourne, Dorothy Adams Campbell and M. Pyke.—p. 608.  
Hereditary Degeneration of Rat Retina. Margherita Cotonio Bourne, Dorothy Adams Campbell and Katharine Tansley.—p. 613.

### British Medical Journal, London

2: 773-820 (Oct. 15) 1938

- Organotherapy. W. Langdon-Brown.—p. 773.  
\*Treatment of Tuberculosis in Guinea Pigs with Sulfanilamide. G. A. H. Buttle and H. J. Parish.—p. 776.  
Sarcoidosis of Boeck. R. B. Scott.—p. 777.  
Further Experiences with Tomography in Pulmonary Tuberculosis. J. B. McDougall and J. H. Crawford.—p. 782.  
Comparison of Clinical and Blood Pictures in Adult Scurvy. G. H. Jennings and A. J. Glazebrook.—p. 784.

2: 821-874 (Oct. 22) 1938

- The State and Medical Research. E. Mellanby.—p. 821.  
Some Aspects of Recent Work on the Bacteriology of Rheumatism. H. J. Gibson.—p. 827.  
Alcohol Injection in Inoperable Malignant Growths of Jaws and Tongue. W. Harris.—p. 831.  
Relation of Hodgkin's Disease and Leukemias to Gastric Disorders. E. Harvey.—p. 833.  
Biologic Significance of Tonsils and Adenoids and Other External Lymphoid Masses. P. W. Leathart.—p. 835.

**Tuberculosis and Sulfanilamide.**—Buttle and Parish found that sulfanilamide inhibited the course of generalized tuberculosis in guinea pigs infected with the human strain of the tubercle bacillus. Their results are less striking than those of Rich and Follis (1938), possibly because of a difference in the tubercle strain. The drug had little influence on the course of infection in guinea pigs and none in rabbits when a bovine strain was used. Further prolonged experimental investigations with sulfanilamide and other preparations are necessary under controlled conditions, and special attention should be paid to the toxicity of the drugs employed.

### Edinburgh Medical Journal

45: 665-740 (Oct.) 1938

- Hemorrhoids and Their Treatment. W. J. Stuart.—p. 665.  
Estrogenic and Androgenic Substances in Pregnancy. A. M. Hain.—p. 678.  
\*\*\*Sprained Ankle." I. S. Smillie.—p. 692.  
The Streptococcal Diseases. S. Thomson.—p. 695.  
Recovery and Rehabilitation. J. Cunningham.—p. 712.

**Sprained Ankle.**—Smillie states that full dorsiflexion is essential for sprained ankle and is best attained by the patient who pulls strongly on the two ends of a length of 1 inch strapping which has been passed in the form of a loop round the foot. The adhesive side of the strapping crosses the sole in the region of the first metatarsal head. While the patient is doing this, a piece of piano felt is shaped to fit in front of and below the lateral malleolus and its bulk is reduced and efficiency increased by beveling the periphery. Three bands of the 1 inch strapping are used for a stirrup type of bandage. These bands overlap one another and are applied parallel to the long axis of the limb. Their overlapping breadth extends from immediately posterior to the base of the fifth metatarsal to the lateral aspect of the fibula. Each band should be applied until the maximal tension is obtained. The upper ends of the three stirrups are secured with two or three circumferential bands of strapping. The felt pad is now placed in position under the

strapping, in the gap between the strapping and the skin. One or two bands of strapping increase the tension on the strapping by being applied circumferentially round the stirrups at the narrow part of the ankle above the medial malleolus. Thus are the artificial ligaments completed. An elastoplast type of bandage is now applied under moderate tension from the roots of the toes to just below the knee. This prevents edema, increases the support and prevents the strapping from slipping. There should be no undue pressure on the base of a prominent fifth metatarsal. The patient is encouraged to use the ankle freely. There is no pain and the foot is stable. At the end of a week a change of support will be necessary, especially if the patient has exercised freely. Healing is usually complete in three weeks.

### Glasgow Medical Journal

12: 173-212 (Oct.) 1938

- Leptospirosis Jaundice: Report of Two Cases with Special Reference to Clinical Investigation. J. C. Middleton and A. J. S. McFadzean.—p. 173.  
Traumatic Asphyxia, with Illustrative Cases. W. I. Gordon and A. M. W. Thomson.—p. 180.

### Journal of Tropical Medicine and Hygiene, London

41: 309-324 (Oct. 1) 1938

- Achromia Flava Amycetica (Pseudo-Tinea Flava, Achromia Flava Tropicalis). A. Castellani.—p. 309.  
Viability of Some Common Pathogenic Fungi. P. K. Fraser.—p. 310.  
Climate, Diet and Toxic Substances in Their Association with Adrenal Condition. A. Clark.—p. 315.  
Intestinal Obstruction and Atrophic Lesion of Appendix Caused by Ascaris. S. Zahawi.—p. 316.

### Lancet, London

2: 813-866 (Oct. 8) 1938

- The Medical Race. R. Hutchison.—p. 813.  
\*Thyroidectomy for the Relief of Cardiac Pain. Report of Twelve Cases. G. Bourne and J. P. Ross.—p. 815.  
\*Macrocytic Hemolytic Anemia Associated with Increased Red Cell Fragility. S. C. Dyke and Freida Young.—p. 817.  
Radiotherapy of Menopausal Menorrhagia and Some Complications. T. F. Todd.—p. 821.  
Osteogenic Sarcoma of Tibia: Survival Thirteen Years After Treatment. C. MacLeod.—p. 824.  
Tuberculosis of the Endocardium in a Case of Hypertension. G. E. S. Ward and N. H. Martin.—p. 827.  
Brevicollis. A. H. Bizarro.—p. 828.  
Spontaneous Hemothorax. K. M. A. Perry.—p. 829.

**Thyroidectomy for Cardiac Pain.**—Twelve patients were relieved of severe angina of effort and spasmodic angina by thyroidectomy. Bourne and Ross believe that the length of time (from three weeks to twenty-six months) that elapsed since the operation proves that this measure is of great and lasting benefit in appropriately chosen cases. Two patients died, one of syncope three weeks and one of coronary thrombosis seven months after the operation. The type of pain most likely to be benefited by thyroidectomy is that of true organic origin, of such severity as to incapacitate the patient and constantly growing worse. Patients with advanced cardiovascular disease are not desirable subjects for thyroidectomy. Adiposity is a contraindication to thyroidectomy, just as thinness is a definite indication. After-treatment must be controlled carefully in order to obtain the best results. Myxedema develops if such patients are completely deprived of thyroid, but if they are too heavily dosed with thyroid extract the pain returns.

**Macrocytic Anemia and Erythrocyte Fragility.**—Dyke and Young describe the common features in six cases of anemia of the macrocytic type. These features are (1) anemia with hemolysis shown by bilirubinemia and a serum van den Bergh reaction of the indirect type, (2) increase in the fragility of the erythrocytes, (3) increase in the mean diameter of the erythrocytes with a consequent high color index, (4) protracted course with remission and relapse, (5) abnormal activity of the hemopoietic system (shown by the presence of numerous nucleated erythrocytes and reticulocytes and by hyperplasia of the bone marrow) and (6) moderate splenic enlargement with endothelial proliferation and phagocytosis of the erythrocytes. This macrocytic hemolytic anemia unresponsive to liver therapy has been identified with congenital acholuric jaundice of the Chauffard type. Actually, the only striking resemblance between them is fragility of the erythrocytes. Their points of dissimilarity are far more numerous. The response to splenectomy of these two types of hemolytic anemia points strongly to the conclusion that

they bear no essential relation to each other. In the Chauffard type the effectiveness of splenectomy has been recognized and the operation does with reasonable certainty bring about disappearance of the symptoms, whereas, from the authors' results in the present series, its value seems doubtful in the acquired type of hemolytic anemia under discussion. Its justification in this condition is debatable.

### Medical Journal of Australia, Sydney

2: 491-536 (Sept. 24) 1938

Inquiry into the Relationship Between the Quality and Kind of Matriculation Passes of Medical Students and Their Subsequent Success or Failure in Various Annual Examinations. F. S. Cotton.—p. 491.

New Line of Treatment in a Certain Type of Arthritis: Preliminary Communication. Eva A. Shipton and L. J. A. Parr.—p. 500.

Precipitin Test Applied to Melbourne Hemolytic Streptococci. Hildred M. Butler.—p. 501.

\*Observations on Diphtheria and Bacterial Types of *Corynebacterium Diphtheriae*. H. Wilson and N. E. Goldsworthy.—p. 509.

2: 537-584 (Oct. 1) 1938

Some Pathologic Changes in Australian Aboriginal Bones. C. V. Mackay.—p. 537.

Treatment of Pneumonia. A. Holmes à Court.—p. 555.

Treatment of Peptic Ulcer by Continuous Drip Method. M. M. O'Brien.—p. 559.

**Types of *Corynebacterium Diphtheriae*.**—Wilson and Goldsworthy isolated 200 strains of *Corynebacterium diphtheriae* from 325 individuals at the Royal North Shore Hospital. Of the 200 patients 109 (five died) were infected by the grave type of *Corynebacterium diphtheriae*, thirteen (one died) were infected by the intermediate type, forty-seven (one died) were infected by the grave type and thirty-one (none of whom died) were infected by atypical strains. Twenty-three strains have been isolated from eighteen patients with malignant diphtheria. Twenty-one cases were of the grave type, in which there were twelve deaths; one was of the intermediate type, in which the patient died, and the last was an atypical type in a patient who recovered. The grave and intermediate types caused on the average more severe disease than the mild type. The relative merits of Löfller's and Clauberg's mediums for the recognition of *Corynebacterium diphtheriae* and of Clauberg's medium and of two kinds of blood agar for the determination of type are discussed.

### Tubercle, London

10: 529-576 (Sept.) 1938

\*Sedimentation Rate in Relation to the Red Cell Count: The Problem of Correction. Norah H. Schuster.—p. 529.

Cadmium: Immediate Results of Its Use in Treatment of Pulmonary Tuberculosis: Review of Forty-Two Cases. V. C. Cornwall.—p. 542.

Postoperative Sequelae of Pneumectomy. A. Behrend.—p. 552.

Pneumothorax Shadows. S. Puder.—p. 557.

### Sedimentation Rate and the Erythrocyte Count.—

Schuster studied the effect of the erythrocyte concentration on the sedimentation rate on 121 individuals. Citrated blood was found to give more consistent results than oxalated blood. In the choice of a tube the diameter (within wide limits) and cubic capacity may be disregarded, but it is essential to have the same height of blood column for a series of tests; 100 mm. is a serviceable height. Polycythemia has a retarding effect on the sedimentation rate and it may disguise a pathologic condition of the blood. Anemia has an accelerating effect, which is magnified in conditions already causing rapid sedimentation. Anemia is occasionally associated with a very slow sedimentation rate. At present the association cannot be attributed to any specific type of anemia. Recovery from anemia with a subnormal sedimentation rate may be associated with a rise in the sedimentation rate. No charted system of correction for changes in the blood count is satisfactory. For special cases and research work the blood count may be adjusted to a standard concentration (say 5,000,000). In conclusion the author states that the sedimentation test as it stands is a useful but crude test for ordinary clinical work; for special investigation it should be done according to laboratory standards of technic and with a proper understanding of the controlling factors, such as the blood count. It is a complicated reaction and not a quantitative analysis. It is sensitive to so many circumstances inside and outside the body that the numerical result should be interpreted with judgment and in relation to the other biologic reactions of the patient.

### Archives de Médecine des Enfants, Paris

41: 609-664 (Oct.) 1938

\*Treatment of Acute Meningitis with Sulfanilamide. L. Tixier.—p. 609.

Disturbances in Acid-Base Equilibrium in Rickets and Tetany. T. Giza.—p. 633.

**Sulfanilamide in Acute Meningitis.**—Tixier, in his service at a children's hospital, employed sulfanilamide with good success in the treatment of cerebrospinal meningitis of various origins. The sulfanilamide preparation employed was para-amino-phenyl sulfamide (1162 F), which is active in vivo and in vitro. The author regards the oral route as the best method of administration and thinks that the intraspinal administration should be reserved for extremely severe cases. The duration of the treatment varies according to the causal agent of the meningitis. René Martin ascribes considerable significance to the sulfanilamide concentration in the cerebrospinal fluid, maintaining that the concentration must be 4 mg. per hundred cubic centimeters. Tixier, however, obtained an extraordinarily high percentage of cures in various types of meningitis without ever testing the sulfanilamide content of the cerebrospinal fluid. Regarding the prophylactic use of sulfanilamide he says that epidemics of cerebrospinal meningitis have been arrested by giving sulfanilamide to exposed persons, such as children, who attended schools in which cases of meningitis occurred. Moreover, he thinks that the treatment with sulfanilamide is justified in cases of suppurating otitis media which do not drain in the usual length of time or in operations on the mastoid which do not cicatrize rapidly, or in other contagious diseases such as grave tonsillitis. Serious complications, especially suppurating meningitis, can thus be reduced to a minimum. The author says that in hundreds of patients treated he never observed a complication of sufficient gravity to necessitate a change in treatment. The cyanosis of the lips and the extremities disappears spontaneously even though the doses of sulfanilamide have not been reduced. In the second part of this report the author takes up separately the various types of meningitis. Under the heading of streptococcal meningitis he first discusses those forms which are secondary to auricular disorders and then the primary forms. Then he discusses and illustrates by case histories the effect of sulfanilamide on meningococcal meningitis, on meningitis without visible microorganisms and on pneumococcal meningitis.

### Bruxelles-Médical, Brussels

18: 1583-1613 (Oct. 16) 1938

\*Limits of Cardiac Activity in Healthy Persons and Patients. Gunther-Zaeper.—p. 1583.

Massive Uterine Gangrene After Delivery. R. Schockaert and J. Brenez.—p. 1590.

### Limits of Cardiac Activity in Healthy Persons and Patients.—

Gunther-Zaeper points out that nearly all the methods utilized so far for the estimation of the functional activity of the heart lack exactness. The author shows (1) that the index of the heart minute volume must be utilized in order to estimate the effective functional activity of the heart and (2) that the oxygen requirements and its transport must be the function of this index, since the transport of oxygen is the most important role of the circulation of the blood. The determination of the absorption of oxygen according to the formula of Fick gives as product the heart minute volume index by the arteriovenous difference in oxygen. This formula shows clearly the significance of the heart minute volume index and its limits in determining the maximum absorption of oxygen and thus the physical capacity. The author established a new method closely related to the procedures of Fick and Plesch, with which he made a series of determinations of circulatory exchanges and of the heart minute volume index. The subject is connected with a metabolism apparatus of Knipping in order to determine the absorption of oxygen. During the work test a stopcock is turned to make the person breathe according to the method of Plesch by means of a mask, the nitrogen passing into a rubber container; in this manner is effected an exchange between the blood which flows from the right side of the heart to the lung and the gaseous mixture arriving in the rubber container, until equalization of pressures

is effected. The venous alveolar air thus obtained is immediately brought into contact with a specimen of blood, withdrawn directly after the assay in a tonometer at the temperature of the body. After the equalization of the gaseous tension the oxygen content is examined in the apparatus of van Slyke. By this procedure the oxygen saturation of the venous mixture of the right side of the heart can be determined indirectly. If after that the arterial saturation is determined either in the arterial blood or in the venous blood that has been saturated with oxygen, it is possible to calculate the difference between the oxygen contents of the arterial and venous bloods. By dividing the figures obtained for the absorption of oxygen by the difference in the oxygen contents of the blood of the right side and that of the left side of the heart, the figure for the heart minute volume index is obtained. The author describes observations with this method on persons who have undergone physical training, on persons who have not undergone such training and on persons with cardiac disorders. He shows that the determination of the respiratory volume and the estimation of the activity of the heart and of the circulation, with the described method, permit a qualitative estimation of the functional capacity of the circulation and the heart.

### Journal de Médecine de Lyon

19: 555-590 (Oct. 5) 1938

- \*Arrhythmia of Patients with Hypertension. A. Dumas.—p. 555.  
Complete Arrhythmia and Rheumatism. L. Gravier and A. Tourniaire.—p. 563.

**Arrhythmia with Hypertension.**—According to Dumas, the severe hypertensions are in general incompatible with arrhythmia. Only extrasystoles, either sporadic or grouped together, are encountered. This extrasystole annoys patients considerably and its treatment is difficult. Complete arrhythmia, on the other hand, is well tolerated by the majority of patients with hypertension. Moreover, recovery from it is accompanied by a reduction in tension; subjectively it is better tolerated than extrasystolic arrhythmia; it does not give rise to pain and when it is accompanied by a slight cardiac insufficiency it can easily be remedied by medication with suitable cardiac tonics. Complete arrhythmia is preferable to the menacing gallop of a regular heart, which maintains a blocked hypertension, capable of provoking either a cerebral hemorrhage or a sudden failing of the heart.

### Presse Médicale, Paris

46: 1505-1520 (Oct. 12) 1938

- Treatment of Clinical Manifestations of Lamblasis. C. Garin.—p. 1505.  
\*Polyglobulism Provoked by Extracts of Anterior Lobe of Hypophysis. Prove Existence of Hemopoietic Hormone. J. Flaks, I. Himmel and A. Zotnik.—p. 1506.

**Polyglobulism and Anterior Lobe of Hypophysis.**—Flaks and his associates state that clinical and experimental observations cited in a previous report indicated that, under physiologic conditions, the hypophysis regulates the hemopoiesis. They attempted to prove that this hemopoietic action of the hypophysis depends on a hormone which differs from the hormones already known. In order to prove the existence of an especial hemopoietic hormone they made investigations in two directions: (1) by ascertaining the atrophy of the hemopoietic tissue of the bone marrow and of the morphogenic elements of the blood, following the ablation of the hypophysis and their reactivation by the administration of hypophysial substance; (2) by provoking a hemopoietic hyperactivity by surcharging the normal organism with supposedly hemopoietic elements. The experiments were made on rats. Discussing the technic they say that the hemoglobin was determined by means of the hemoglobinometer of Hellige and the number of erythrocytes with Thomas's apparatus. The reticulocytes, which were colored with brilliant cresyl violet, were counted in the humid chamber. The bone marrow was extracted from the femur immediately after the animal had been killed. The hypophysis was extirpated after trepanation of the base of the cranium by means of a small vacuum pump. Observations on the variations in the blood elements in normal rats show that the number of erythrocytes never exceeds 9.5 millions.

Consequently, the authors regard as polyglobulism those values of erythrocytes which exceed 10 million. Polyglobulism is the test for the demonstration of the hemopoietic hormone. Hypophysial substance was administered to hypophysectomized as well as to normal rats. On the basis of these and of earlier experiences the authors reach the conclusion that it is justified to admit the existence of a hemopoietic hormone in the hypophysis.

### Schweizerische medizinische Wochenschrift, Basel

68: 1153-1180 (Oct. 15) 1938. Partial Index

- Remarks on Topographic Anatomy of Pulmonary Nerves at Level of Hilus in Human Subjects. A. Baumann.—p. 1156.  
\*Remarks on Exploration of Renal Function in Scarlet Fever. P. Gautier.—p. 1161.  
Surgery of Peripheral Nerves. A. Jentzer.—p. 1162.  
Regarding Urobilinuria in Alcoholic Patients. R. de Montmollin.—p. 1165.  
Relation Between General Arterial Tension and Retinal Arterial Tension in Psychiatry. F. Morel, A. Franceschetti and E. B. Streiff.—p. 1166.  
Cutireaction with Diphtherial Toxin, Test of Sensitivity to Diphtheria. T. Reh.—p. 1173.  
Insulin in Nonschizophrenic Psychic Disturbances. J. E. Staehelin.—p. 1175.

**Renal Function in Scarlet Fever.**—Gautier reports studies on azotemia in fifty children. He lists the average azotemic values during the first five days, from the sixth to the tenth day, from the eleventh to the fifteenth day and from the sixteenth to the twenty-first day. This list indicates that the values were highest during the first five days. However, this early azotemia has no connection with the scarlatinal nephritis. Moreover, the general condition in the course of scarlet fever seems to exert no great influence on the azotemia. The author also cites observations on albuminuria and on the elimination of urea in the urine of children with scarlet fever. He says that he performed Volhard's test systematically in twenty-six children with scarlet fever. On the basis of the results he differentiates seven groups of patients. In the first group, which comprised six children, the test was at once normal. In the second group (four children) the test revealed abnormal results with regard to the diuresis. However, repetitions of the test revealed gradual subsidence of the functional disturbance. In the third group (one case) the first test revealed abnormal conditions as regards the diuresis as well as the dilution. In the fourth group (seven cases) the test revealed abnormalities in the diuresis and the concentration. The functional disturbance disappeared before the end of the scarlet fever in all these cases. In the fifth group (two cases) the test revealed abnormal diuresis, concentration and dilution. In the sixth group (three cases) the test still revealed abnormalities during the fourth repetition. In this group the clinical observations gave no satisfactory explanation for the abnormal outcome of the test. The seventh group includes the patients with previous renal lesions caused by a former nephritis. The cases cannot be compared with the others. The author reaches the conclusion that Volhard's test, if performed systematically, often reveals in one of the stages of the disease a functional disturbance of the kidney which is usually mild. The results obtained with the two methods of renal examination (study of azotemia and Volhard's test) confirm that it is necessary to keep the renal function under careful observation in the course of scarlet fever.

### Bollettino d'Oculistica, Florence

17: 693-800 (Sept.) 1938. Partial Index

- Familial Hereditary Dystrophy of Cornea with Recurrent Erosive Degeneration of Epithelium. M. Berardi and A. Motolese.—p. 711.  
Spectrography for Presence of Metals in Conjunctiva. G. Bietti.—p. 729.  
\*Behavior of Ocular Tension in Course of Hypoglycemic Coma. G. Ciotola.—p. 738.  
Estrogenic Substance in Therapy of Gonorrheal Conjunctivitis. D. Borioni.—p. 776.

**Ocular Tension in Hypoglycemic Coma.**—Ciotola observed the ocular tension in the course of hypoglycemic coma in eleven patients with schizophrenia. Determinations of the tension were made at half hour intervals during the first four hours in the course of various attacks of insulin coma. Ocular hypotension was present in all cases. In some it amounted to 12 mm. of mercury. According to the author,

ocular hypotension is proportional neither to the amount of insulin which is administered to the patients nor to the amount of sugar in the blood in the course of the shock. The behavior of the factors which regulate the ocular tension is similar in diabetic and hypoglycemic coma with the exception that the blood pressure is diminished in the former and increased in the latter. In both cases the hypotonic factors are the loss of water of the body with consequent thickness of the blood and increase of the osmotic colloidal pressure. A diminished blood supply of the eyeball and the presence in the blood serum of substances which are toxic for the capillaries of the eye are hypotensive factors of secondary importance. In the course of hypoglycemic coma two factors which follow an opposite direction are present. They are the aforementioned hypotonic factors on the one hand and the increased blood pressure on the other. The latter tends to prevent intra-ocular hypotension. When the former factors predominate over the latter, which is in the majority of cases, ocular hypotension takes place. In the course of diabetic coma the hypotensive local and general factors, including the local and general blood pressure, which is diminished, tend to the production of ocular hypotension, which takes place in all cases of the condition.

### Tumori, Milan

12: 281-454 (July-Oct.) 1938. Partial Index

- \*Estrogenic Substances in Skin and Relation Between Estrogenic and Androgenic Substances. E. Silvestroni.—p. 281.
- Histogenesis of Plasmocytic Myeloma. U. Teodori.—p. 295.
- Angioplasmic Glyoblastoma and Cysts of Encephalon: Case. C. Rizzi.—p. 363.
- Gastrointestinal Carcinoids: Case. S. La Manna.—p. 381.

**Estrogenic Substances in Skin.**—Silvestroni's experiments were made in an effort to ascertain the presence of estrogenic substances in irradiated skin and the relations between estrogen and androgen. He experimented in various lots of adult female castrated rats. He found that estruation does not appear in adult female castrated rats after injections of (1) extracts of irradiated skin of adult male rabbits and male rats which had had repeated progressive ultraviolet or roentgen irradiations on the back, (2) of extracts of the whole testicle of adult animals, (3) of liposoluble or hydrosoluble testicular preparations and (4) of transplantation of testicles. Testosterone alone does not induce estruation, which appears during the first two or five days in the course of the associated treatment of testosterone and estrogen and then stops. According to the author the skin irradiated by either ultraviolet or roentgen irradiations does not contain estrogenic substances. When the latter are present in certain organs, especially in the testicle of certain animals, they originate in disintegrated estrogen which is taken in the food and transformed by the body.

### Revista de Tuberculosis del Uruguay, Montevideo

7: 113-200 (No. 2) 1938. Partial Index

- Indications for Discontinuation of Artificial Pneumothorax. C. B. Netto.—p. 153.
- Costa Test in Pulmonary Tuberculosis. F. D. Gomez and J. L. Vilar Del Valle.—p. 157.
- \*Sedimentation Speed of Erythrocytes and Vernes' Sero-flocculation in Diagnosis of Evolution of Tuberculosis. F. D. Gomez, A. R. Gines and J. C. Benítez.—p. 162.
- Pneumoperitoneum in Treatment of Pulmonary Tuberculosis. F. Gómez and J. L. Vilar Del Valle.—p. 175.

**Diagnosis of Evolution of Pulmonary Tuberculosis.**—Gómez and his collaborators followed the results of the sedimentation speed of the erythrocytes and of Vernes sero-flocculation test in 200 patients suffering from pulmonary tuberculosis. Both tests show the evolution of the pulmonary tuberculous lesion and give parallel results in the majority of cases. However, the resorcinol flocculation test shows aggravation or amelioration of the pulmonary lesion earlier than the sedimentation test. Negative results of the flocculation test in the presence of positive results of sedimentation show a favorable evolution of the pulmonary lesion in the near future. The opposite also takes place. Syphilis and pregnancy have no influence on the results of the flocculation test. Both conditions cause acceleration of the sedimentation of the erythrocytes.

### Deutsche Zeitschrift für Chirurgie, Berlin

251: 1-124 (Sept. 23) 1938. Partial Index

- Operative Treatment of Fractures of Head of Tibia with Central Depression of Portion of Joint. F. Lichtenauer.—p. 1.
- \*Experimental Production of Sarcoma with Radium and Mesothorium. E. Uehlinger and O. Schürch.—p. 12.
- \*Practical Application of Chronaxia in Surgery. Y. Osawa and I. Nagai.—p. 34.
- Histogenesis of Epulis. H. B. Sprung.—p. 64.
- Five Year Cures in Sarcoma. O. Dyes.—p. 77.

**Experimental Sarcoma from Radium and Mesothorium.**—Uehlinger and Schürch carried out in the course of seven years 107 experiments in rabbits in which a mixture of 0.005 mg. of mesothorium in petrolatum was placed in the thoracic cavity, the cavity of the shaft of the femur, the spleen, the liver, the stomach wall and the testis. Of the twenty-one rabbits in which implantation was made into the femur, fourteen exhibited a metastasizing sarcoma; of the three in which radioactive substance was placed in the spleen, one; of the five with implantation into the liver, one; of the eight with implantation into the gastric wall, two; of the seven with implantation into the testicle and nine into the pleura, none. The lethal period for bone sarcoma vacillated between twenty-one months and fifty months, for sarcoma of the internal organs between twenty-one months and twenty-nine months. It appeared that the carcinogenic property was equally shared by the pure alpha, beta and gamma rays. However, the sarcoma developing after the implantation of radioactive substances is to be regarded as the result of collective irradiation. The pure, free alpha mesothorium rays possess equal cancerigenic properties with radium so far as the latent period and incidence of tumor formation are concerned. The variation in the dose of mesothorium between 0.0001 and 0.005 mg. had no effect on the frequency of tumor formation or on the latent period. The effect of the radioactive substances was primarily on the connective tissue and only exceptionally on epithelial structures. With the exception of the central nervous system, no predisposition was noted on the part of any organ. The radiation sarcoma corresponds biologically and histologically to the spontaneous sarcoma. The authors predict that with the increase in the radiation treatment of tumors there will be a corresponding increase of sarcomas as the result of radiation damage.

**Chronaxia in Surgery.**—Osawa and Nagai have investigated chronaxia values in 683 patients with brain, spinal cord and peripheral nerve lesions. The observations were confirmed in most of the cases at operation. Chronaxia values in mild pathologic alterations showed a diminution or an insignificant increase, whereas in far advanced pathologic lesions the increase was great. Chronaxia values of peripheral nerves frequently are definitely increased. Changes were observed both in brain and in spinal cord lesions. However, in brain lesions they are insignificant. Chronaxia determinations enable one to make a localizing diagnosis of the lesion. The extent of the lesion and its right-sided or left-sided localization are possible in the injuries of the peripheral nerves. Chronaxia determinations are particularly valuable in cases in which the clinical symptoms are not clear. Chronaxia observations were negative in cases of simulation and neurosis. The authors believe that this method permits of more accurate diagnostic determinations than the previous methods.

### Monatsschrift für Kinderheilkunde, Berlin

75: 177-405 (Sept. 29) 1938. Partial Index

- \*Dietetic Treatment of Alimentary Toxicosis in Nurslings During First Three Months of Life. W. Bayer.—p. 177.
- Oil Milk. G. Frontali.—p. 189.
- Value of Determination of Bacillus Carriers and of Persons Continuing to Excrete Bacilli for Prophylaxis of Infectious Diseases. H. Kleinschmidt.—p. 224.
- Mesenchymal Dysplasia and Pylorospasm. P. Kroeger.—p. 247.
- Question of Dosage for Therapeutic Diphtheria Serum. K. Noster.—p. 289.
- Pathogenesis of Tuberculosis of Cervical Glands. H. Opitz.—p. 294.
- Duodenal or Gastric Ulcer and Umbilical Colic. A. Peiper and E. Hofmann.—p. 306.
- \*Studies on "Rounded Back" and Funnel Chest. K. Stoltz.—p. 358.

**Alimentary Toxicosis in Nurslings.**—Bayer discusses the treatment of the severest form of alimentary toxicosis, the form in which the toxic symptoms are completely developed and in which there are signs of cerebral disturbances, such as

dulled sensorium or complete stupor; retardation in the conduction of pain and in the defense reactions; uncoordinated movements of the eyes; instead of vigorous crying, low whimpering and unmotivated loud cries; and slow, dragging movements of the extremities. In the seventeen cases on which the author made his observations there were three fatalities. The age of the child is a determining factor in the prognosis of alimentary toxicosis: with increasing age, the danger to the life decreases. That the previous nutrition is an important factor in estimating the severity of the process is proved by the fact that the majority of the nurslings had received no breast milk at all and others had received inadequate amounts of it. The author says that, like all severe intoxications, alimentary toxicosis should be treated in a hospital. His therapeutic efforts aim at preventing a further loss of weight, rapid detoxication and the prompt absorption of fluids. He regards it as advisable to leave the gastrointestinal tract strictly alone for a while, alimentation by mouth being stopped for from twelve to twenty-four hours. The first alimentation consists of a modified Ringer's solution, small quantities of which (20 or 30 Gm.) are given at first every hour, but later at longer intervals. Then the alimentation with Ringer's solution is changed to feeding with whey and a 6 per cent rice gruel, which are mixed in a proportion of 1 and 2. Sugar is not added to this mixture. The author is of the opinion that caloric foods such as protein, fat and carbohydrate should not be given too early by mouth. Fats and proteins in the form of breast milk or buttermilk are only slowly added to the whey-gruel mixture. At first the nursling is given only one-third breast milk but gradually three feedings of whole breast milk and two feedings of half buttermilk with 5 per cent sugar are introduced. The author says that the nutritional intake is slowly increased because inanition is no longer feared as much as it was formerly. Moreover, during the first days of the treatment the infusions are the indispensable factor in the treatment. The nurslings are given by intravenous injection a mixture of Ringer's and of a dextrose solution. This mixture is always freshly prepared. The more severe the intoxication, the smaller should be the amount of dextrose in the solution. The infusions are continued beyond the end of the fasting period, but they are gradually decreased as the oral intake is increased. In the first few days from four to six infusions of from 50 to 100 cc. each are given during each twenty-four hour period. The infusions are given mostly into the cranial veins, but they can be given also into the veins of the dorsum of the foot and hand. If during the severe collapse it is too difficult to reach a vein, the first injection may be made into the longitudinal sinus.

**Rounded Back and Funnel Chest.**—Stolte says that the majority of investigators regard the "rounded back" as the result of a deficient muscular development. It cannot be denied that a rounded back may be the result of a weakness of the skeletal musculature, but he does not think that this applies to all cases. He raises the question whether the weakness of the musculature and the fatigability of such children may not perhaps have another cause. He points out that the entire habitus of these children, with their narrow thorax, their rounded back and their prolapsed abdomen corresponds to that of the patients who, as the result of an enteroptosis, develop a drop heart. Moreover, the observations in the course of roentgenoscopy suggest a malproportion between the growth of the heart and of the vertebral column, and the rounded back seems to act as a compensatory mechanism for this malproportion. Good care and nutrition occasionally make up for the retarded development of the heart and, if this is so, the rounded back has a tendency to disappear. In the second part of his paper the author discusses the development of a funnel chest. After citing the two generally accepted theories of the development of a funnel chest he describes his own observations, which convinced him that the traction of the abdominal muscles, particularly the proper function of the abdominal rectus, is of great importance for the development of the thorax. He shows that this muscle represents, in a way, an elastic, extraordinarily adaptable prolongation of the sternum, which by its traction is capable of compensating the depression of the sternum. If this muscle is weakened, the diaphragm alone acts on the sternum and thus the funnel chest is produced.

## Münchener medizinische Wochenschrift, Munich

85: 1497-1536 (Sept. 30) 1938. Partial Index

Indications and Prognosis of Operation for Senile Cataract. R. Braun.—p. 1497.

\*Problem of Habitual Abortion. M. Kneer.—p. 1501.

Treatment of Pulmonary Embolism. K. L. Müller.—p. 1505.

Exercise Splint for Active Treatment of Deformities of Leg. H. Schwan.—p. 1507.

Hemoptysis in Mitral Stenosis with Especial Consideration of Other Pulmonary Hemorrhages. O. Scheurer.—p. 1514.

Experiences with Böhler's Treatment of Vertebral Fractures in Small Hospital. G. Becker.—p. 1519.

**Problem of Habitual Abortion.**—Kneer says that, although many factors have been suggested as possible causes of habitual abortion, in many cases it proves difficult to find a satisfactory explanation. In this paper he reports investigations on 110 women who were subject to habitual abortion. Among this number there were only eight in whom anatomic changes on the genitalia gave a satisfactory explanation for the repeated abortions, and in another woman it appeared probable that a mitral insufficiency was the cause of repeated abortions. In the others the examination at first revealed nothing that would explain the repeated abortions. However, investigations on the menstruation revealed that a considerable number of the women, particularly those who habitually aborted during the first few months of pregnancy, had disturbances of the ovarian function, particularly in the formation of the corpus luteum. Others again had a habitus which suggested secretory disturbances and some of them had also a genital hypoplasia. The author shows that in another group of cases the inferior biologic character of the fetus is responsible for the abortion; it appears that in these cases the expulsion of the fetus is a manifestation of a biologic self protection of nature. Such a possibility must be taken into consideration, particularly in abortions that take place after the fourth month of gestation and in cases in which the parents are related. In this connection the author cites cases of women who in first marriages had given birth to healthy children, whereas in second marriages, with men to whom they were related, they were subject to habitual abortion. The author admits that in this report he failed to mention vitamin deficiency, heterogenic character of blood groups and other factors which have been mentioned as possible causes of habitual abortion. He says that in the material under consideration there was no definite proof that the latter factors had assumed a causal role in the habitual abortions.

## Zeitschrift f. d. ges. experimentelle Medizin, Berlin

104: 121-248 (Sept. 19) 1938. Partial Index

Action of Analeptics on Circulation. H. W. Bansi, M. Kalinke and J. Schilling.—p. 121.

Reduction in Cholesterol Ester Following Administration of Prehormone (Gonadotropic Hormone Obtained from Pregnancy Urine) and Its Modification. E. Fenz and F. Zell.—p. 138.

\*Change of Serum Phosphatase in Cancer Patients and Its Use in Diagnosis. D. Albers.—p. 146.

Allergic-Hyperergic Gastritis: Experiments on Animals. T. C. Afendulis and M. Gölzow.—p. 167.

Progesterone and Hair Growth: Experimental Study. G. Hensel.—p. 182.

Pathogenesis of Gastric and Duodenal Ulcers. R. Nothhaas.—p. 188.

Quantitative Investigations on Porphyrin Metabolism in Healthy Persons and Patients: Decomposition of Chlorophyll. J. T. Brugsch.—p. 210.

**Serum Phosphatase in Diagnosis of Cancer.**—Albers directs attention to the fact that the phosphatase content of the blood of patients with cancer is different from that of normal persons. In order to determine whether these changes have diagnostic value he determined the phosphatase values in the serum of eighty-six patients with cancer and of forty-one control persons. He employed the method of Jenner and Kay, which is based on the phosphatase activity of the plasma; that is, on its ability to hydrolyze sodium beta-glycerophosphate. The author found that in cases of carcinoma the phosphatase values of the serum are generally increased. Since the determination of the phosphatase values alone is not adequate for the diagnosis of cancer, he decided to test the mechanisms of activation and inhibition as well. For the activation he employed a magnesium chloride concentration and for inhibition a calcium lactate concentration. It was found that the



activation was increased in the presence of cancer, whereas the inhibition showed no noticeable differences when compared with that of the controls. In most of the disorders found in the controls, the phosphatase values were low. However, jaundice, ulcers of the gastrointestinal tract and pulmonary tuberculosis were exceptions. In nonmalignant tumors and tumor-like diseases the phosphatase values varied. Two cases associated with lymphogranuloma and two with benign tumors revealed high phosphatase values and increased activation, whereas in sarcomas and leukemias the phosphatase values were low. In utilizing the phosphatase activity of the serum and its activation or inhibition as the basis of the diagnosis of cancer, the author considered as positive those serums in which the phosphatase values were in excess of 17 units or the activation was at least 60 per cent; as negative those serums in which the phosphatase values were below 16 and the activation was less than 60 per cent. The values between 16 and 17 units and the activation between 55 and 60 per cent were regarded as doubtful. The tables indicating the phosphatase values of the examined serums show 85 per cent of positive (that is, correct) results in the cases with carcinoma and 69 per cent negative (that is, correct) results in the controls. In cases of carcinoma associated with established metastatization the correct results were 97 per cent. Cases of jaundice, gastrointestinal ulcer and tuberculosis were excluded from these estimates.

# Geneeskundig Tijdschr. v. Nederl.-Indië, Batavia

78: 2299-2360 (Sept. 20) 1938. Partial Index

- \*Leptospirosis in Australia and Some Remarks on Determination of Types of Isolated Strains. B. Walch-Sorgdrager, L. Bohlender and W. A. P. Schöffner.—p. 2299.
- Age of Marriage and Births in Chinese Women of the Lower Middle Class in Batavia. L. P. Kian.—p. 2309.
- Secondary Pellagra. K. J. Pronk.—p. 2340.

**Leptospirosis in Australia.**—Walch-Sorgdrager and his associates state that cases of leptospirosis have been reported from three different parts of Australia from the districts of Ingham, Pomona and Brisbane. In each district the spirochetosis had its peculiar aspect and causal agent. In the Ingham district spirochetosis occurs endemically with epidemic aggravations among cane cutters. Mild and serious cases were observed there with and without jaundice, and among the latter group there were some fatal cases. Ballica and Zandoni strains were found to be the causative agents and the first of these proved to be a new kind of leptospira; the second, although reacting with the Salinem group, should probably be regarded as a separate strain. Both strains were found also in the rat. In Pomona, cases of a mild, seven day fever occur every year. In one case the Pomona strain was cultivated, a strain which has not been described before and which has its own antigenous nature. In Brisbane three cases of leptospirosis were described, two of which concerned sewer workers. These were classic cases of leptospirosis icterohaemorrhagica. The author discusses some of the difficulties that were encountered in connection with the classification of the Zandoni strain. Serologic tests on the Zandoni and Salinem strains indicated that in their antigenic structure these two strains are partly identical. However, further studies will be necessary to decide whether the Zandoni strain belongs to the Salinem group or not. The authors think that for the present the Zandoni strain should be designated as Australis B, the term applied to it by Lumley.

# Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

82: 4411-4486 (Sept. 10) 1938. Partial Index

- Phacomatoses. J. van der Hoeve.—p. 4418.
- \*Influence of Vitamin C on Course of Tuberculosis of Bones and Joints. E. H. J. Warns.—p. 4426.
- Significance of Determination of Alcohol Content of Blood for Detection of Infringement of Article 22 of Law Regarding Motor and Bicycle Traffic. J. Zeldenrust and P. H. Teunissen.—p. 4435.
- Perinephric Abscess with Perforation Toward the Intestine (Renal Caruncle?). W. E. Jak.—p. 4444.

# Vitamin C in Tuberculosis of Bones and Joints.—

Warns reports studies on twenty-six patients with tuberculosis of the bones and joints. Sixteen of these patients had spondylitis, four had coxitis, five had gonitis and one had a clavicular

tuberculosis. Six had at the same time tuberculosis of other parts of the skeleton. Vitamin C was administered to these patients by mouth in the form of tablets, each of which contained 50 mg. of a synthetic ascorbic acid. At the onset the dose was 250 mg. for adults and for children over 6 years of age; it was 150 mg. for children less than 6 years of age. As soon as the urinary concentration reached more than 5 mg. per hundred cubic centimeters, the dose was decreased to 50 mg. a day. The saturation with the vitamin C was continued for four and one-half months. A therapeutic action on the tuberculous process could not be detected; however, it seemed that the general condition was slightly improved. Like other investigators, the author observed that patients with tuberculosis have greatly increased vitamin C requirements, their daily consumption being from three to five times as much as in healthy subjects. Moreover, there seems to be a certain parallelism between the quantity consumed and the activity of the process.

# Acta Chirurgica Scandinavica, Stockholm

81: 99-308 (Sept. 16) 1938. Partial Index

- Diagnosis of Fibrous Pericarditis. S. Ingvar.—p. 99.
- Fibrous Pericarditis and Its Surgical Treatment. E. Tengwall.—p. 118.
- Primary Psoriasis: Five Cases. E. Schroeder.—p. 139.
- Radical Treatment of Carcinoma of Rectum. T. Eiken.—p. 155.
- Fracture of Calcaneus. H. S. Nissen-Lie.—p. 186.
- Isolated Gonorrheal Tendovaginitides. R. Wilenius.—p. 195.
- \*Conditions and Results of Injection Therapy on Varices and Clinical Anatomical Study of Relapses. K. Mårtensson.—p. 237.

**Injection Therapy of Varices.**—Mårtensson says that the immediate results of the injection therapy of varicose veins are generally regarded as good but that the opinions on the later results differ greatly. With the aid of the Trendelenburg-Berntsen test, which gives exact information about the changes in the cutaneous veins, the author made observations on 102 patients with progressive insufficiency of the veins of the legs, all of whom had been subjected to ambulatory injection therapy. In the course of these control tests, which extended over a period of three years, the author found that the relapses occurred only in cases in which immediately or soon after the blockage a centrifugal venous current developed on the level with or proximally to the thrombus. The relapses originated from destruction of the thrombosis and the recanalization or formation of a passage as well as from the refilling of veins that had not been thrombosed but only collapsed. The refilling with blood was effected by a remaining proximal portion of an insufficient vein either directly or by way of an insufficient collateral. Relapses developed in all cases (fifty-five in all) in which the insufficiencies of the veins of the lower leg extended above the lower third of the thigh. The relapses occurred earlier and were more extensive in cases in which only a small portion had been blocked than in cases in which blockage had been as extensive as possible. The varying degrees of venous insufficiency seemed to make no difference in this respect. All relapses developed between one and eighteen months after completion of the treatment. The relapses generally resulted in a greater or lesser extension of the insufficiency; it was most pronounced in cases of partial blockage and in three cases it was followed by the development of new varicose ulcers. Relapses did not occur in forty-five cases in which the venous insufficiency was restricted to one or two branches of a vein. Histologic studies in these cases revealed that the factors favoring relapses are completely eliminated. Moreover it seems that, if the injection therapy is executed properly, the further extension of the venous insufficiency can be arrested at least for a while (time of observation). In these cases the injection treatment was easy and did not result in complications. On the basis of the results of this study the author concludes that cases in which the venous insufficiency is restricted to venous branches in the lower part of the leg (all early cases of varices) require only injection therapy, provided of course that the injection treatment is not contraindicated by other disorders. In all other cases, that is, in those in which the insufficiency of the veins has been extended to the thigh, the combination therapy according to De Takáts-Quillin should be employed. In some cases in which the exact differentiation is difficult, the injection treatment should be followed by the combination therapy.

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## THE RATIONAL TREATMENT OF ACUTE HEMATOGENOUS OSTEOMYELITIS

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ST. LOUIS

The clinical picture and laboratory observations in acute hematogenous osteomyelitis are so well known to the average physician that a discussion of the diagnosis in this paper is not warranted. However, in a large percentage of the cases the diagnosis is not made until late in the disease. This is because the general practitioners and pediatricians who see the early cases are not osteomyelitis conscious. Consequently I would like to emphasize the facts that when a child suddenly becomes ill with fever and presents evidence of pain, disability and localized deep tenderness in an extremity osteomyelitis should be considered, and a negative x-ray examination does not rule out this disease.

This paper is presented because the disease is relatively frequent and not only carries a high mortality but usually causes prolonged illness in many of those who survive the acute attack and is an important factor in the production of crippling. While most surgeons have definite ideas as to the proper treatment of acute osteomyelitis, the treatment advised by authorities on the subject varies from that of the radical group, who recommend immediate emergency operation with adequate drainage of the focus in the bone, to that of the conservative group, who treat the patient for the general infection and more or less ignore the focus in the bone with the expectation that, as the patient's resistance is increased, the local disease will either heal spontaneously or form a subcutaneous abscess which can be drained by a small incision. There are, of course, all gradations between these two extremes, and a rather extensive study of recent literature leaves one very much confused. It is thought, then, that a rational consideration of the disease may tend to harmonize some of the wide differences of opinion.

The disease is caused by pyogenic bacteria which enter the blood stream from some focus (demonstrable in about 20 per cent of the patients) or are present as causal organisms in the blood stream and localize in the bone and begin to multiply. More than 90 per cent of the cases that occur are in children and it is generally believed that the usual site of the primary infection in the bone is in the metaphysis near the epiphyseal line.

In infants under 2 years of age the offending organism is a hemolytic streptococcus in about half of the cases and a staphylococcus in almost all of the remainder. In children over 2 years of age about 90 per cent of the cases are due to *Staphylococcus aureus*, and the streptococci account for most of the remainder. Either of these organisms may kill the patient promptly by an overwhelming general infection or more slowly over a period of weeks or may lead to prolonged suppuration with necrosis of bone, or an abscess may form which drains and heals or which heals without drainage.

It is thus obvious that there may be wide variations in the course and prognosis of individual patients, each of whom is suffering from an acute hematogenous osteomyelitis. These are due to that poorly understood condition which may be called the relation of the patient's resistance to the virulence of the organism. An increase in the patient's resistance or a decrease in the virulence of the organism will tend to cure the disease, and the converse also is true. Consequently, since "the first duty of the physician is to do no harm," care must be taken not to do anything to lower the patient's resistance even temporarily unless sufficient benefit will accrue to justify the procedure. It is accepted that an operation tends to lower the patient's resistance temporarily and that the ill effects vary directly with the amount of blood lost, the extent of the operation, the time consumed in performing it and the duration of the period of anesthesia.

The pyogenic cocci are characterized by their invasive qualities and by their ability to kill the tissues which they invade. This ability to spread into and kill the surrounding tissues is most evident when the focus is confined in the tissues and is relatively slight when the focus is on a surface or is adequately drained so that the growth of the organisms and the reaction of the tissues cannot generate pressure.

In the subcutaneous tissues infection with pyogenic cocci results in an acute inflammation. As the bacteria increase in number the adjacent cells are killed, autolysis occurs and pus is formed. The extravasation of fluid in the tissues, the dilatation of the blood vessels and the accumulation of phagocytic cells, especially leukocytes, and the proliferation of connective tissue cells cause swelling and tend to wall off and localize the infection. When the process occurs in a nonexpansible compartment, such as a bone, the changes mentioned are inhibited and the bacteria are enabled to invade and destroy the surrounding tissues with greater facility. It is also to be noted that in the subcutaneous tissues pain and tenderness occur early, while in the bone the focus is silent until the inflammation has reached the periosteum, because the interior of the bone is devoid of sensation, as can be demonstrated by infiltrating the

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periosteum with procaine hydrochloride and drilling through the bone without causing pain.

It is thus apparent that by the time the infection causes pain and local tenderness the inflammation has spread through the cortex to the periosteum and that early drainage of the focus in the bone is desirable in order to inhibit the spread of the infection in the bone and the resultant extensive necrosis of bone. Early drainage of the focus in the bone is desirable not only because it tends to limit the local spread of the infection in the bone but also because it tends to cut off the supply of organisms at its source.

This brings up the question as to what is meant by the terms bacteremia and septicemia. I formerly considered bacteremia a condition in which bacteria were being fed into the blood stream from a focus and were being destroyed at about the same rate as that at which they entered the blood; the term septicemia I applied to a more severe condition in which the bacteria were actually multiplying in the blood stream. This distinction was purely theoretical and has been abandoned; and the two terms are used interchangeably to refer to a state in which bacteria enter the blood stream more rapidly than the defense mechanisms of the organism can destroy them, and it is probable that in certain instances the blood serves as a culture medium and the organisms actually multiply in the blood stream.

The source of the organisms in the blood stream is not an academic question but is of great practical importance because it determines the therapy in acute osteomyelitis. A large number of otherwise competent observers hold that since the bacteria reached the bone through the blood stream the patient is suffering primarily from a general infection and that the focus in the bone is merely incidental and should be ignored while the physician directs his therapy to the general infection. I have no patience with such reasoning. These patients were not sick until the focus developed in the bone, and they are now sick because they have a spreading infection in the bone which is feeding toxins and possibly bacteria into the circulation. If they have a demonstrable primary focus this merely served as a means by which a few bacteria got into the blood stream. It is not to be thought of as a funnel pouring a steady stream of bacteria into the blood. Had these few bacteria been taken care of in the usual way, nothing would have happened. But when some of them settled in the bone and started a spreading infection the disease began.

It is thus evident, I believe, that the local lesion should be drained. The next question is When should it be drained? It is argued that in the early stages the condition in the bone is analogous to a spreading cellulitis and that it is a fundamental principle of surgery not to incise a spreading cellulitis but to immobilize the part and apply local heat until the infection has localized and local tissue immunity has been established. By local immunity is meant a local concentration of opsonins which affect the bacteria in some manner and render them susceptible to the phagocytes. I do not believe that it has been established that there is sufficient local concentration of antibodies around a pyogenic infection to be of clinical importance. It is my impression that the localization of a pyogenic infection is an anatomic rather than an immunologic phenomenon and that it is due to the concentration of leukocytes and connective tissue cells and to the mechanical factors of vascular dilatation, edema and thrombosis. In a nonexpansile compartment, such as bone, there is con-

siderable difficulty in the mechanical walling off of an infection, and the thrombi become septic and aid rather than hinder the spread of the disease.

While I do not recommend it, I do not believe that any particular harm is done by incising an area of cellulitis provided the tissues are not unduly traumatized and the part is treated properly afterward. In draining a deep abscess one incises through normal tissues and then a zone of cellulitis and is not concerned with the possibility of opening up blood or lymph channels that will permit the infection to reach the blood stream, nor is one concerned that the organisms from the deep abscess will invade and destroy the overlying normal tissues which have not established a local immunity. When the infection is in a tendon sheath or a joint it is drained immediately and one does not wait for these structures to be destroyed while the patient's resistance is increased to a point at which an equilibrium between it and the infection is established. Why should it be different in bone?

Furthermore, it is to be noted that infections in bone are not seen by surgeons as early as are severe infections in soft tissues, because the focus is silent until it spreads through the bone to the periosteum where it can affect sensory nerves and because the physicians who see them early are not osteomyelitis conscious and do not make the diagnosis early. In a series of 200 consecutive patients with chronic osteomyelitis who were admitted to the Shriners' Hospital for Crippled Children in St. Louis, Dr. McCarroll and I found that forty-one in whom an incorrect diagnosis had been made had been under treatment for from one to twelve weeks and that only nine had had the bone drained during the first week of the disease. It is thus evident that relatively few of these patients enter the hospital or are seen by a surgeon during the early stages of their illness, and the abscess in the bone is usually well established when they enter the hospital.

The question then arises as to whether they should be operated on immediately or treated conservatively. It is obvious that in a disease which varies so greatly in its severity and in its course the treatment cannot be standardized and that each patient must be considered as an individual problem which must be met according to the best principles of surgery.

#### CLASSIFICATION OF PATIENTS

From the standpoint of treatment, patients with acute hematogenous osteomyelitis may be divided into four overlapping groups: (1) patients with a mild infection who are not acutely ill, (2) severely ill patients with a spreading infection but in good general condition, (3) severely ill patients with a spreading infection and in poor general condition, and (4) patients in whom the infection has localized and is subsiding.

1. The treatment of patients who are not acutely ill need not be an emergency affair, but there is no reason why these patients should not be operated on and the bone drained as soon as convenient after the diagnosis is made. As a rule, these are patients in whom the infection is of relatively low grade, in whom there is very little danger that it will be widely disseminated in the bone and in whom the infection may form an abscess which can be drained subsequently or may even form an abscess in the bone which will heal spontaneously if they are left alone. On the other hand, if these patients are not treated a localized chronic osteomyelitis may develop which will demand radical treatment.

Consequently, I think it advisable to operate on such patients and drain the focus in the bone early in order to prevent the probable later chronic disease.

2. The severely ill patients with a spreading infection of the bone with high fever and marked toxemia are those seen relatively early in the disease but who are not dehydrated and whose general condition is good. A blood culture should be taken on admission, but one should not wait for the result, because it has no influence on the immediate treatment, which should be directed to the focus in the bone. In these cases I believe that waiting is not advisable because the pyogenic organisms are characterized by their tendency to invade and necrotize surrounding tissues, and if the patients are not operated on there will probably result a widespread destruction of bone with eventual development of a chronic osteomyelitis which may be difficult or impossible to heal. In addition to this there is the danger of involvement of the joint and the development of metastatic foci of infection. There is also the definite danger that leaving the abscess in the bone will tend to the production of a septicemia.

It is to be noted that I do not consider that a patient in whom hematogenous osteomyelitis develops has a primary septicemia but I feel that the septicemia which is so frequent in this disease is secondary to the infection in the bone. In other words, the constant presence of organisms in the blood stream means that these organisms are being fed into the blood stream more rapidly than the system of the patient is able to get rid of them and does not necessarily mean that one organism has got into the blood stream and has continued to multiply. The continued presence of the infection in the bone under pressure is one of the most favorable conditions for the development and continuance of such a septicemia, and even if a septicemia is present one of the most efficient methods of combating it is to cut off the supply of organisms to the blood stream by draining the focus in the bone. In such cases I recommend immediate operation with opening of the bone as gently as possible and with as little disturbance to the patient as possible. Under these conditions I have used local anesthesia and added epinephrine to the procaine hydrochloride and have found it possible to drain bony abscesses with but little harm to the patient.

After the operation the wound should be packed loosely with petrolatum gauze and the extremity should be immobilized in a large, hot, wet dressing and splint or in a plaster-of-paris cast, and fluids should be forced, if possible, or given intravenously or subcutaneously if necessary. Sufficient morphine or other sedative should be given to relieve the pain. To severely ill patients we have usually given repeated small transfusions and have not seen harm result from them, but I doubt whether they do any particular good in acute infections when there has been no significant loss of blood from the operation and when sufficient time has not elapsed for the production of a secondary anemia by the infection. Later, if a secondary anemia develops, transfusions are indicated to restore the blood volume or replace the cells that have been destroyed, but I am skeptical as to their value in supplying antibodies to combat the infection.

In infants under 2 years of age somewhat more leeway is allowed, and the operation may be delayed for four reasons: 1. The bone is more porous and the infection can more readily pass out through the bone and form extraosseous abscesses without sequestration.

2. Infants become dehydrated and toxic very quickly and most of them are badly in need of fluids when first seen. 3. Infants do not stand surgical operation as well as do older children and adults. 4. There is about an even chance that the infecting organism is a streptococcus which is susceptible to sulfanilamide.

3. Severely ill patients not in good general condition are usually patients who have had the disease for some time and are extremely toxic, are frequently delirious, are markedly dehydrated and have a high fever and a rapid, thready pulse. There is frequently a positive blood culture on admission. On this type of patient it is unwise to operate immediately, not because it is not desirable to drain the focus in the bone but because the patient's resistance is very low and has been taxed to the breaking point by the infection. Consequently it is better to put such a patient to bed, relieve his pain by morphine and immobilize the extremity, preferably with the application of a massive hot, wet pack and a splint with traction if it is practicable to do so. Fluids should be given immediately by mouth if possible or in the form of dextrose or salt solution intravenously if necessary.

If the patient is under 2 years of age there is about an even chance that the offending organism is a streptococcus and sulfanilamide in rather large doses may be started immediately without waiting for the blood or aspiration culture. This is because infants tolerate the drug well and because we delay operating on infants under conditions in which an older child would be operated on immediately. In children over 2 years of age we do not give the drug until we have obtained a positive culture of a streptococcus, because the chances are less than one in ten that it is a streptococcus and I believe that sulfanilamide may actually do harm in staphylococcal infections. Certainly I do not like the idea of operating on patients who are cyanotic from the drug, and these patients are going to be operated on because even in streptococcal infections I do not believe that it has been shown that sulfanilamide has much effect on a focus in a bone. In my limited experience it has not cleared up such foci, though it is possible that it may have helped to localize the disease.

In addition to the foregoing, one must consider immune serum, antitoxic serum, bacteriophage and toxoids. Bacteriophage has been recommended especially for staphylococcal septicemia. However, MacNeal's<sup>1</sup> figures give a mortality rate of 70 per cent, which is about the usual mortality of staphylococcal septicemia without bacteriophage, and since bacteriophage is inactive in blood serum I do not believe that it is worth while to try it.<sup>2</sup> Toxoids and vaccines are of no value in an acute infection and of questionable value in a chronic staphylococcal infection because, as is well known, the human organism shows little or no tendency to develop an immunity to the staphylococcus. The same is true of transfusions with blood from patients who have recovered from a similar disease or who have chronic osteomyelitis. These patients do not, in my experience, carry a high degree of immunity to the staphylococcus. In streptococcal infections it may be possible to find donors with sufficient opsonins to be of value, and if laboratory facilities and sufficient donors are available they should be checked for opsonins

1. MacNeal, W. J., and Frisbee, Frances C.: One Hundred Patients with Staphylococcal Septicemia Receiving Bacteriophage Service, *Am. J. M. Sc.* 191:179-195 (Feb.) 1936.

2. Eaton, M. D., and Bayne-Jones, Stanhope: Bacteriophage Therapy, *J. A. M. A.* 103:1769-1776 (Dec. 8), 1847-1853 (Dec. 15), 1934-1939 (Dec. 22) 1934.

against the offending organism and immunotransfusions should be given as suggested by Lyons.<sup>3</sup> Robertson<sup>4</sup> used an immune serum which he believes to be of some value. It should be given intramuscularly and not intravenously, since seven of Robertson's nine patients to whom it was given intravenously died. There is a staphylococcus antitoxin on the market and it is hoped that it will be of value in detoxifying these acutely ill patients; it may be used in large doses in order to get them into condition for operative drainage. Its use is still in the experimental stage.

The question next arises as to how long one should continue conservative treatment. This cannot be stated, but I believe that one should continue such treatment a matter of twelve hours or so until the patient appears to be getting better or worse. As soon as the patient has had some sleep and rest from the morphine and immobilization and as soon as his body fluids have been restored, I think that he should be operated on whether or not an abscess is present, provided a competent surgeon is at hand to perform the operation. The point is, I regard the deferring of the operation not as an attempt to permit the infection to localize but only as an effort to get the patient into better condition for the operation. Consequently, the waiting period is a matter of hours rather than of days.

4. In the last group of patients, in whom the infection has broken through the bone and formed an extra-osseous abscess and whose acute illness is subsiding, I do not think it makes very much difference when they are operated on. However, the sooner the abscesses are drained the less likely are secondary foci to develop, although it is probable that by the time the acute condition has begun to subside there will be no further destruction of the bone. They really present a problem in chronic osteomyelitis and represent the group who have survived the so-called conservative treatment.

#### TYPE OF OPERATION

The type of operation varies with the condition found and with the age of the patient. In infants as little work as possible should be done on the bone. In children and adults it is important that adequate drainage of the focus within the bone be accomplished. It is stated that this can be done adequately by incising the periosteum. Starr<sup>5</sup> and his co-workers advocate drilling the metaphysis near and in the direction of the epiphyseal line. If one is going to expose the bone I think that it does no harm to take out a window, especially as one is taking the window from the metaphysis where the cortex is quite thin, and if one uses sharp, thin osteotomes or large drills this can be done with relatively little trauma. The cavity is not curetted and no effort is made to remove the dead bone. The operation is for drainage only and is not a sequestrectomy. This gives a much better exposure of the underlying cancellous bone and is less apt to damage the epiphyseal line. In confirmation of the likelihood of damaging the epiphyseal line by drilling according to the method of Starr, Johnson's<sup>6</sup> report of seventy-three cases in which this method was used showed that there was disturbance of growth in 55 per cent.

3. Lyons, Champ: Immunotransfusion and Antitoxin Therapy in Hemolytic Streptococcus Infections, *J. A. M. A.* 105: 1972-1975 (Dec. 14) 1935.

4. Robertson, D. E.: Acute Hematogenous Osteomyelitis, *J. Bone & Joint Surg.* 20: 35-47 (Jan.) 1938.

5. Starr, C. L.: Acute Hematogenous Osteomyelitis, *Arch. Surg.* 4: 567-587 (May) 1922.

6. Johnson, R. A. Y.: Effect of Inflammation on the Epiphyses, *Arch. Surg.* 32: 810 (May) 1936.

In very ill patients the anesthetic should not be started until the surgeon is ready to make the incision, the operation should be as simple and brief as possible, and especial care should be taken not to traumatize the tissues unduly and a tourniquet is not applied.

After the operation the wound should be packed loosely with petrolatum gauze and the extremity immobilized either in a very large hot, wet dressing or in a plaster-of-paris cast, and the preoperative treatment just described should be continued.

In a diffuse infection in cancellous bone it is impossible to drain all of the area. Consequently, the temperature may be expected to fall gradually unless a septicemia is present. In certain cases the temperature will fall and then rise after a few days. This may be due to inadequate drainage of the primary focus, to extension of this focus or to the development of another focus. If another focus develops it should be drained as soon as it is recognized if the patient's condition warrants the operation. In cases in which drainage is established very early, and especially in those due to streptococci, the primary wound may heal without sequestration. In cases due to a staphylococcus in which there has been widespread destruction of bone there will be sequestration and chronic osteomyelitis which must be treated at a later date.

#### CONCLUSIONS

1. Early diagnosis is as important as it ever was in pyogenic infections of bone, and each case should be treated as an individual problem and according to the surgical principle that a deep abscess should be drained as early as possible provided the patient is in condition to stand the operation.

2. Not every case of acute osteomyelitis requires immediate operation, but every patient with this disease presents an acute surgical emergency and should be seen by a surgeon as soon as possible after the onset of the disease. The surgeon should decide when to drain the focus in the bone, and this decision may be a difficult one.

3. Early and adequate drainage of acute osteomyelitis is the most effective means of preventing chronic osteomyelitis.<sup>7</sup>

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#### ABSTRACT OF DISCUSSION

DR. W. D. GRIESEMER, Reading, Pa.: Dr. Key has given his treatment of this disease in a complete manner. Not all men will be in complete agreement with his views. Since most of these cases occur in children, diagnosis is often delayed until a period that precludes effective early treatment. The type and severity of the infection influence the treatment. In treatment, one may run the gamut from extreme conservatism to some form of radical procedure. The latter may vary from simple incision of the periosteum to drilling the medullary cavity or to extensive chiseling operations, with removal of the diseased cortex for drainage. Extreme conservatism is supported by a number of writers. A more radical course is advocated by others. However, nothing radical is done until local suppuration is very certain. Pyogenic osteomyelitis is not considered a surgical problem until this occurs. Fulminating cases, with few localizing signs, are fatal in spite of any treatment. In these one feels equally wrong in being radical or in just standing by. However, one should not in a routine manner delay primary operation, awaiting very marked local signs. Such surgical inactivity will increase an already appalling mortality.

7. Key, J. A.: The Prevention of Chronic Osteomyelitis: Early Diagnosis and Treatment of Acute Osteomyelitis, *J. Missouri State M. A.* 33: 39-43 (Feb.) 1936.

Neither should operation be extensive as a matter of routine. Its extent should be indicated by conditions found. Conservative, intelligent, exploratory operation with due consideration of all factors appears to be the best course and certainly can do no harm. Dr. Key's paper is a contribution to the treatment of these difficult cases.

DR. JESSE T. NICHOLSON, Philadelphia: Dr. Key has presented many of the perplexities encountered in the treatment of acute hematogenous osteomyelitis. He has given a classification of cases. He has found immediate operation necessary in but one group, the severely ill with a spreading infection but in good general condition. He has emphasized the role of the local bone focus as a source of toxin and bacteria which influence the general condition of the patient. These undoubtedly would be good reasons for immediate radical operation, but the results of conservative care and delayed operation make even these points controversial. In reviewing some of the recent papers on osteomyelitis one obtains the impression that early operation is hazardous to the patient. Green and Shannon found a mortality of 45 per cent following operation in infants under 6 months, and 21 per cent for all children under 2 years. They called attention to the high incidence of streptococcal infection at this age. This type of infection results in spontaneous formation of superficial abscesses and absence of sequestrum. By treating the general infection with blood transfusions, administration of increased fluids and simple incision of the abscess when it formed, the mortality was decreased to 3 per cent. Wilson and McKeever reviewed ninety cases including children over 2 years of age. In this group the staphylococcus was the common cause of the infection. When surgical drainage was done in the first seven days there was a 25 per cent mortality and after one week 9.7 mortality; in twenty-three cases in which spontaneous drainage occurred there was only one fatality. Even more conclusive was the recent report of Henry Brown of 160 cases before the Philadelphia Academy of Surgery. In the very toxic group, in which immediate operation was done, the mortality was 34 per cent. In very toxic cases in which surgery was delayed the mortality was 11 per cent. In the group of nontoxic cases there was no difference in mortality whether operation was immediate or delayed. The autopsies in cases in which death followed early operation proved by the evidence of multiple abscesses that the surgical procedure was futile. In the presence of blood stream infection there was a 51 per cent mortality. In cases in which a secondary blood stream infection developed following operation a 52 per cent mortality resulted.

DR. JOHN C. WILSON, Los Angeles: The situation resolves itself into treatment of infection irrespective of whether or not a bone abscess is present. Dr. Key said to me "You went so far in your paper as to advise the patients not to see a doctor." I do feel that when an abscess develops it should be drained, but all are familiar with cases of osteomyelitis that are opened in the first twenty-four or forty-eight hours in which no pus is encountered. The medullary canal contains a gray or serous exudate from which a positive culture of staphylococcus or streptococcus may be recovered. Those are the cases in which drainage should not be done. Whether or not septicemia is a primary or secondary factor is beside the point. An early drainage of these infections in the bone will, if the bacterial count in the blood culture is carefully observed, cause it to rise. I have seen this happen on a number of occasions. I have been following the bacterial count from day to day, and immediately after the drainage of the abscess the number of colonies per cubic centimeter of blood is markedly increased. It is my belief that the patients should be observed at least for a short time or until one finds out how the organism as a whole is reacting to this generalized infection. Blood cultures are of value to determine whether or not the patient is reacting properly. A gradual or rapid increase in the number of organisms recovered per cubic centimeter of blood indicates very closely that the patient's resistance is low. I cannot agree with Dr. Key that incision of a cellulitis or an infection which is not localized is without danger. Incision of a brawny, indurated area of skin and soft tissue is associated with great hazard. A little later on when this area softens and an abscess is formed it may be drained with impunity. The same situation occurs in bone. When the pus is present it should be evacuated, but all are

aware that the evacuation of the abscess in the bone does not produce an immediate drop in temperature. It sometimes continues as long as six weeks after the drainage of the medullary canal before the temperature drops to normal. The plea that I wish to make is for the consideration of the patient as a whole and not of the individual bone lesion. The use of sulfanilamide has been mentioned. It probably has some place in the treatment of streptococcal infections but before using it one should know the type of organism that caused this particular difficulty. During the past year I have used immune rabbit serum in a few patients, apparently with some satisfactory results, but this must be continued for a further time before definite conclusions may be drawn.

DR. EARL D. MCBRIDE, Oklahoma City: I am seeing osteomyelitis in a much earlier stage and at a much younger age than I used to. It seems to me one ought to add just one more qualification to the type of common sense treatment. If the patient is a child in whom the abscess has already found its exit through the cortical bone but has not drained through the subfascial tissue or through the skin, it seems to me useless to expose the child to the dangers of an operation to open the bone further. One should simply drain the abscess of soft tissues under a local anesthetic and not try to do anything to the bone until a later date. After the child has regained strength, further drainage of the bone may be necessary. However, if it can be decided that the bone has not released the pressure by exit of its own accord, the bone should be drained surgically at that early stage in as cautious a manner as possible.

DR. WALTER G. STERN, Cleveland: I should like to ask Dr. Key whether he does not believe that in the stage of the disease which Dr. Wilson discussed—just before the abscess forms—if one just took a good, big, sharp, rotating burr and went into that area and out as quickly as one could, would one not, in an absolutely harmless manner, create a channel out of which the pus, when formed, may be readily drained, eliminating all tendency to back pressure and thus relieve the children of the danger of having those multiple foci that I so deplore?

DR. CHARLES F. NELSON, Beverly Hills, Calif.: The question of nutrition has been neglected in the discussion of the osteomyelitis situation. Why do these children have osteomyelitis? The reason is a developmental disturbance plus the lack of proper nutrition which is the vitamin and mineral balance. In my work on bone metabolism I have come to believe that a normal bone is never infected. Mineral imbalance probably precedes any bone disease. I have implanted staphylococci taken from cultures of osteomyelitis with septicemia into bone in animals, and the animals which have been kept on diets containing mineral and vitamin balance for a few weeks before the implantation suffered no ill effects while animals prepared on insufficient diets died. Osteomyelitis usually develops in children who are suffering from rickets or have some osteoporosis. The osteoid tissue present has almost no circulation. Without bone trabeculae there are no capillaries and this is the site where infection begins. Physicians should be reminded at once to establish vitamin and mineral balance, as marked general improvement of the child can be influenced immediately and local resistance about the foci of infection can be thrown out in a few days by the establishment of trabeculae with their accompanying capillaries. Most children with osteomyelitis have a latent tetany and their mineral balance should at once be established. I feel that the factor of developing resistance should be stressed. The question of drainage is an individual one. One should use every means of general sustenance until some definite evidence of localization has been established and then one should not be too destructive with surgical operation.

DR. J. ALBERT KEY, St. Louis: During the past year Dr. McCarroll and I reviewed 200 patients with chronic osteomyelitis who had been patients in the Shriners' Hospital, St. Louis. Of the 200 patients 50 per cent had joint involvement, 25 per cent had multiple foci, and 33⅓ per cent of the total number that we were able to treat over a period of three years were not cured at the end of three years. In other words, we cured only two thirds of those patients, and we could do anything that we wanted to with them. I may also add, for the benefit of the statistics, that we had no mortality among any of those patients, which I think is one answer to the mortality in statistics which



is seen elsewhere. Patients who enter with abscesses don't die. The patients of this group who were going to die died before they got to the hospital. The die is cast early in the disease in a certain number of persons who develop an acute pyogenic infection and there is nothing that anybody can do that will save them. There is also a group that are going to get well in spite of anything that we can do. There is a much larger group in whom we may influence the course of the disease. Early operation, if possible before pus is formed, will abort a considerable number of these cases of acute osteomyelitis, will prevent patients from getting extremely toxic and will save a lot of crippling in children. If the patient is too toxic to stand the operation, I think that one must wait until one can get the patient in as good condition as possible, not because one wants an abscess to form but because one wants to be able to operate on a patient who has a chance of surviving.

### TREATMENT OF FRACTURE-DISLOCATION OF THE SPINE ASSOCIATED WITH CORD INJURY

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Injury to the cord by fracture-dislocation of the spine frequently demands that consideration be given to measures which will protect the cord from further injury by pressure of displaced bone. The impossibility of regeneration of the cord being accepted, it logically follows that the treatment of cord injuries, so far as restoration of function of the cord is concerned, is effective only in those cases in which the cord has not been entirely destroyed at the level of the vertebral lesion.

It is often stated that, because of the concussion and spinal shock associated with severe injuries to the cord produced by fracture-dislocation, it is impossible to make an early differentiation between complete physiologic interruption which may later show some recovery and a total transverse lesion which is permanent.<sup>1</sup>

It seems improbable that concussion is a factor of importance in cases of fracture-dislocation due to indirect violence. A better explanation of the instantaneous loss of function is contusion or crushing of the cord in the pia, which is rarely lacerated except in the most severe injuries. Laminectomy cannot improve the condition of the injured cord in such cases.

Compression of the cord is determined by the Queckenstedt test. The importance of this test in the study of injuries of the spinal cord was emphasized by one of us<sup>2</sup> in 1925. At this time we considered a positive subarachnoid block, demonstrated early by the Queckenstedt test, as an unequivocal indication for operation, unless the dislocation was so extensive as to show conclusively that the cord was crushed. Before the application of this test to the study of cord injuries

there was little reliable data on which the indications for laminectomy might be based, and in many cases operation was done when there was no pressure on the cord. In the absence of compression on the cord, operation is not only futile but increases the damage to the spinal column already weakened by the injury. A larger experience with the Queckenstedt test has removed an earlier optimism with respect to the performance of laminectomy in those cases in which a fracture-dislocation has been suffered with immediate loss of all function of the cord below the site of the dislocation.

Examination of the cord at operation in complete lesions nearly always shows a sleeve of pia mater enclosing a softened, pulpy mass of disintegrated cord tissue, and pressure over the contused area after incision of the dura permits the finger to palpate the body of the vertebra with no resistance other than that offered by the pia alone.<sup>3</sup> In no case in our series has compression been due to extradural or extramedullary blood clot, although gross blood in the spinal fluid has been present in about one half of the cases. In a few cases due to direct force, the laminae are fractured and may be driven in on the cord. Fractures of the laminae with displacement and compression of the cord are more hopeful as a rule than fracture-dislocation. In severe incomplete cord lesions with compression from fractured laminae, prompt laminectomy may be of great benefit.

Partial or complete recoil of the displaced vertebrae toward normal alignment is the rule in fracture-dislocation of the spine. The greatest displacement continues only so long as the displacing force is in action, and the damage to the cord is generally completed when the dislocation reaches its maximum. On partial or complete recoil of the displaced vertebrae, bony pressure is reduced and may in some cases be completely removed from the injured cord. X-ray examination after recoil can give no information as to the extent of the displacement when the force was acting, so the gravity of the lesion must be determined by the patient's history and the evidence of impairment of function of the peripheral cord.

The history which the patient with a complete lesion usually gives is that with the impact of the injury he became paralyzed and lost all sensation in the lower extremities. If examination of the patient discloses absence of the Babinski reflex, deep sensibility, tactile sensation and deep reflexes distal to the lesion, our experience indicates that the injury to the cord is a hopeless one regardless of the treatment employed. The only recovery in such cases has been the return of some segmental innervation just below the level of the injury. For some years we have considered immediate and complete physiologic interruption of the cord from fracture-dislocation produced by indirect violence as an equivalent of anatomic transection.

Unconsciousness from an associated injury to the head or the mental confusion that sometimes results from lesions high on the cervical spine may render the patient incapable of giving an accurate history as to whether the injury produced complete and instantaneous loss of function of the cord below the lesion, and in some cases in which there is no unconscious state, mental confusion may make the tests for sensory and motor impairment

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Read before the Section on Orthopedic Surgery at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

1. Spiller, W. G.: A Critical Summary of Recent Literature on Concussion of the Spinal Cord, with Some Original Observations, *Am. J. M. Sc.* 118, 1899.

2. Coleman, C. C.: Determination of Local Compression as an Indication for Laminectomy in Acute Injury of the Spinal Cord, *J. A. M. A.* 85:1106-1109 (Oct. 10) 1925; Further Observations on Spinal Block in Acute Cord Injury, *Tr. South. S. A.*, 1925; contribution in *Operative Acute Cord Injury*, Horsley, J. S., and Bigger, I. A., editors, Vol. 2, St. Louis, Surgery, Horsley, J. S., and Bigger, I. A., editors, Vol. 2, St. Louis, C. V. Mosby Company 2: 1302-1311, 1937.

3. Thompson, J. E.: Pathological Changes Occurring in the Spinal Cord Following Fracture Dislocation of the Vertebrae, *Ann. Surg.* 78: 260 (Aug.) 1923.

unreliable. In such cases, provided there is pressure on the cord as demonstrated by the Queckenstedt test, it seems permissible to resort to operative measures to relieve the pressure, with the hope that the injury did not crush the cord and that the relief of pressure might result in some benefit to the patient. Cases of this type are unusual, but, in the absence of history indicating that the onset of paralysis was instantaneous, one may be justified in assuming that it was not immediately complete.

Spinal injuries are often overlooked in unconscious patients. The stiffness of a broken neck has frequently been attributed to the bloody spinal fluid from an intracranial injury until the persistent complaint of the patient after recovery from unconsciousness led to adequate x-ray studies. Injury of the cervical spine is so frequently associated with a combined injury of the head and shoulder that special attention should be given to the cervical spine when the unconscious patient has also sustained a fractured clavicle or injury to the shoulder girdle. We have seen a considerable number of cases in which there was a combination of head, cervical spine and shoulder injury.

Cord lesions from fracture-dislocation are rarely progressive. Experience shows that the maximum damage to the cord is usually manifested immediately, and, if the cord has not been crushed, considerable recovery extending over a long period may be expected. It is highly probable that the inherent tendency of the partial lesion to recover much of the function temporarily lost deserves the larger share of the credit for improvement following operation or manipulative procedures which decompress the spinal canal or restore vertebral alignment. It is difficult to evaluate the effect of operation in incomplete lesions, but certainly there is good reason to believe that the improvement in many cases due to the processes of repair has been erroneously attributed to laminectomy.

When we first applied the Queckenstedt test in 1923 for the determination of compression of the cord in cases in which there was complete paralysis, it was hoped that prompt relief of pressure would restore some function of the cord, and for a number of years laminectomy was done in all cases if the patient's condition permitted. The results have shown the operation to be futile in these cases for the reason that the damage is maximal at the time of impact and restoration of function is therefore impossible.

No satisfactory explanation can be offered here for the reported recovery after laminectomy of the occasional patient who is said to have immediately lost all cord function below the level of injury, but it may be suggested that an accurate history probably could not be obtained in these cases or that the neurologic examination was incomplete. It may also be that the criteria of a complete cord lesion as recognized by some writers might have been classified as incomplete by others. We have regarded an early positive Babinski reflex in the absence of any other signs of cord function distal to the lesion, as evidence that the lesion is not complete.

Herniation of the intervertebral disk into the spinal canal caused by fracture has been found in our series of injuries to the spinal cord. If the resulting cord lesion is instantly complete from the impact of the dislocated disk, it would seem that the prognosis would be practically the same as that of a complete lesion

from fracture-dislocation in which the cord was crushed by displaced bone. The absence of x-ray evidence of deformity of the spinal column in severe injuries to the cord does not necessarily mean that a posterior dislocation of the cartilage has injured the cord. Vertebral recoil following extensive dislocation may have taken place, giving a practically normal roentgenogram, but the cord lesion may nevertheless be permanent.

#### USE OF SKELETAL TRACTION

Skeletal traction for the treatment of cervical fracture-dislocation suggested itself to one of us (C. C. C.) in June 1932 as a procedure of necessity in a case of telescoping fracture-dislocation of the axis on the third cervical vertebra without injury to the cord. Ordinary halter traction, so unsatisfactory as a method of cervical extension, could not be employed in this case because of an associated compound fracture of the skull and a compound comminuted fracture of the mandible. After weighing carefully the importance of reducing the exaggerated dislocation and the impossibility of applying traction by the methods then in use, we decided that the circumstances in the case required the application of extension tongs to the skull for the reduction of the dislocation. Edmonton tongs were applied to the skull in this case by our associate Dr. W. G. Crutchfield. It was obvious from the beginning that this type of traction was far more comfortable than that which we were accustomed to apply. X-ray examination showed widening of the intervertebral spaces and partial reduction of the dislocation by the skeletal traction. Functionally the results were excellent.

The principle of skeletal traction having been established, a most ingenious apparatus for the application of this type of traction in cervical injuries was devised by Dr. Crutchfield, and this apparatus carries out in a simple and more effective manner all the principles of the original conception. The technic of application and the results to be expected from skeletal traction by skull tongs have been discussed by Dr. Crutchfield<sup>4</sup> in a series of papers.

We have substituted skeletal traction for laminectomy in cases of complete cervical injuries with dislocation. We have seen no improvement in the function of the cord from the use of skeletal traction in these cases, and in this respect it has achieved no more than laminectomy. Skeletal traction, however, is a very minor procedure and carries practically no risk. It will reduce the dislocation and relieve the root pains, which may be very troublesome in some cases. It has therefore been used in complete lesions for the reduction of dislocation and relief of root pains and as a compromise between the futility of laminectomy and the policy of complete inaction, which is so unsatisfactory to the patient and his relatives.

#### INCOMPLETE LESIONS

The treatment of incomplete lesions of the cord offers a field for useful surgery provided there is pressure on the cord. Incomplete lesions of the cervical region with fracture-dislocation may be treated by skeletal traction for from eighteen to twenty-four hours. After this time, if the cord lesion is stationary or increasing and the block continues, laminectomy is indicated. In cases of cervical dislocation with mild

4. Crutchfield, W. G.: Skeletal Traction for Dislocation of the Cervical Spine, *South. Surgeon* 11:156-159 (June) 1933; Fracture-Dislocations of the Cervical Spine, *Am. J. Surg.* 38:592-598 (Dec.) 1937.

or no injury to the cord, reduction of the dislocation by skeletal traction is the ideal treatment. Recurrence of the dislocation may be prevented by appropriate orthopedic measures.

A subarachnoid block caused by cervical fracture-dislocation, in our experience, is not usually removed even though the dislocation is completely reduced by skeletal traction. With regard to incomplete cord injuries of the dorsal or upper lumbar region, we are not prepared to express an opinion as to the effect of hyperextension on a subarachnoid block, since we prefer laminectomy as a primary procedure in such cases. It should be said, however, that a review of the literature indicates that hyperextension in the treatment of compression fractures of the dorsal and lumbar regions with associated injury of the cord or cauda equina is often satisfactory. It appears that hyperextension in some hands has superseded laminectomy in the treatment of these cases.

Restoration of the alinement of the vertebral column at any level may leave a contused swollen cord compressed and incarcerated by the dura. The continuing block after reduction of the dislocation may be demonstrated by the Queckenstedt test. In such a situation there would not be complete relief of circulatory impairment in the contused cord segments, and as a result an incomplete lesion might become progressive. If symptoms of impairment of the cord are not ameliorated by reduction of the dislocation, or if the symptoms should increase and the block continue, indications for laminectomy are as urgent as if there had been no reduction of the dislocation.

The fear of producing further injury to the cord by manual reduction of a cervical dislocation in partial injuries is well founded, and it is difficult also to free one's mind of considerable apprehension for the fate of the cord when compression fracture-dislocations of the dorsal and upper lumbar regions with incomplete cord injury are reduced by hyperextension. If the dorsal canal has been narrowed by the injury and particularly if there is a fracture of the laminae or pedicles, further encroachment on the canal, however slight, from manipulation of the vertebral segments, might result in an increase of paralysis or even a total loss of cord function. The withholding of an anesthetic during the manipulation incident to manual reduction of cervical dislocations or hyperextension of the dorsal and lumbar lesions is of little protection against further injury to the cord. Should pressure on the cord be suddenly increased by the manipulation, the damage is instantaneous, just as in the case of complete lesions from fracture dislocation in which the crushing of the cord is coincident with the impact of the dislocating vertebra. The gradual unlocking of a cervical dislocation by skeletal traction is not attended by the risk of further injury to the cord. In this respect it is in marked contrast to manual reduction of cervical dislocations and hyperextension procedures for the relief of dorsolumbar lesions.

It is of some importance to determine the proper sequence of the steps in the treatment of incomplete dorsal injuries, associated with compression fractures. It would be most helpful to know whether a severe incomplete lesion with pressure on the cord can be more safely managed first by hyperextension and then by laminectomy if the compression is not relieved, or whether the order of these procedures should be

reversed. Because of the limitation of x-ray studies in disclosing the position of the fragments of bone and their possible encroachment on the dura, it must be assumed that evidence of complete block associated with fracture-dislocation is an indication that further encroachment on the cord may result in increased damage to this important structure. For this reason it would seem safer in these cases to perform a laminectomy to give greater protection to the cord before hyperextension is attempted. There should be little hesitation in using hyperextension for reduction of deformity in immediately complete lesions of the dorsal cord. The correction of deformities due to compression fracture and dislocation, particularly in the lower dorsal and lumbar regions, is highly desirable even with irreparable cord lesions because of the longer duration of life and the wider range of activities which these patients may have, as contrasted with complete lesions of the upper dorsal and cervical regions. It is true that the reduction of a dislocation above the cauda equina cannot be expected to bring about improvement in those cases in which the lesion shows immediate and complete loss of cord function, but hyperextension may restore the column to normal alinement and prevent root pains.

Laminectomy for injuries involving the cauda equina is not restricted by the limitations which experience has imposed in the treatment of lesions of the cervical and dorsal cord. The cord, being a solid cylindric structure, is more vulnerable to a compressing force than the bundle of roots which comprise the cauda equina. Moreover, the cauda equina has a greater capacity for resisting the effects of injury, and the motor roots possess the power of regeneration under favorable conditions even after severe injury or complete division. The relief of compression, while not benefiting the sensory roots already destroyed, may protect others not so badly damaged from progressive injury due to pressure of a deformed column. Laminectomy is therefore indicated in fracture-dislocation of the lumbar spine involving the cauda equina, even when a complete nervous lesion appears to have been immediately produced. Delay in operating on lesions of the cauda equina is likely to add to the damaging compression complications due to formation of adhesions, making an adequate operation extremely difficult or even impossible.

The technic of laminectomy for injuries to the cord may be briefly considered. The greatest care is necessary in handling the patient and transferring him to the operating table to avoid further injury to the cord. Local anesthesia is generally satisfactory and is preferred, especially in cervical operations. In injuries high on the cervical spine the use of morphine should be avoided. Before the operation the fluid below the compression is removed by lumbar puncture and replaced by air. The disclosure of the subarachnoid air after the dura is opened promptly indicates that the lower level of the compression has been relieved, while the free escape of fluid from above shows that the highest level of the compression has been removed. In fracture of the laminae the greatest care is necessary in separating the attachment of the muscles and in removing the bone to avoid further damage to the cord. Wide separation of the muscles from each side is generally unnecessary and should be avoided whenever possible. Hemorrhage from the muscles is controlled

entirely by the electrocautery, and in no operation is this equipment more useful. The level of the greatest bone compression is usually determined by x-ray study before operation and verified by the appearance of the column after operative exposure. The laminae adjacent to those of the displaced vertebrae are first removed and the arch compressing the cord is reserved for removal last, as an added protection to the underlying cord. Incision of the dura should begin above or below the level of compression and continue until the constriction of the cord is entirely relieved. In some cases of pressure by fragments of laminae it is unnecessary to open the dura. If opened, however, and this is usually required in confusion of the cord, no effort is made to suture the dura. In some cases traction combined with simultaneous pressure over the displaced vertebra in the proper direction may restore alignment during the laminectomy. Drainage is rarely required.

After cervical laminectomy, the head, neck and upper part of the chest should be immobilized by a plaster shell extending from the occiput to the lower lumbar region. The advisability of fixation in hyperextension after laminectomy for dorsal and lumbar injuries should be determined in consultation with the orthopedist.

#### MANAGEMENT OF SEVERE INJURIES

The general management of patients with severe cord injuries is obviously of the greatest importance. Pressure sores may be prevented by careful nursing and the use of cork or air mattresses. The complication of bedsores and infection seriously retards the progress of an incomplete lesion, delays or prevents the advent of an automatic bladder in the complete lesions and adds enormously to the problems of nursing care and expense of treatment. In our series of cases various methods of management of the paralyzed bladder have been tried. Intermittent catheterization, the use of a retention catheter, allowing the bladder to overflow, and suprapubic cystostomy have all been given a fair trial. The value and disadvantages of all these methods have been carefully considered, and we have adopted suprapubic cystostomy with drainage as a routine measure for all male patients with paralysis of the bladder due to an injury to the cord. This method has seemed to give the patient a greater protection from infection of the bladder and kidneys, and at the same time it has simplified the general nursing care of the patient. A retention catheter is nearly always followed by some form of genito-urinary infection in the male, but it is entirely satisfactory in the paralyzed female patient.

In our clinics all patients with a spinal injury are admitted primarily to the neurosurgical service. If the patient has a cord injury, a careful neurologic examination together with adequate x-ray study and the Queckenstedt test is promptly made to determine whether laminectomy is required. It may be necessary to repeat the Queckenstedt test several times before a decision can be made as to whether operation is indicated. Cases showing no involvement of the cord are transferred to the orthopedic service. All hyperextension procedures for injuries with or without associated impairment of the cord are conducted by the orthopedic department. Our urologic and orthopedic colleagues have generously cooperated in the management of these cases.

In a series of 259 consecutive patients admitted to one of our clinics (Medical College of Virginia) in a five year period ended Jan. 1, 1938, during which

time skeletal traction for cervical dislocation was originated, there was a group of eighty patients with cord lesions or root injuries involving important peripheral nerves. The location of these lesions was as follows: fifty-three cervical, fourteen thoracic and thirteen lumbar. There were thirty-one patients with complete cord lesions, twenty-four of whom died in the hospital. There was no improvement in the function of the cord in any of these cases. There were forty-nine incomplete cord lesions with twelve hospital deaths. Associated injuries rather than the cord lesion were responsible for death in a number of the latter cases. The incidence of associated injuries was high (twenty-four cases).

Laminectomy was performed in ten of the eighty cases analyzed in this paper. There were five laminectomies in the cervical region and five below this level. Of the cervical laminectomies, four were fatal or unimproved. The case in which there was improvement was incomplete and presented a subarachnoid block as the indication for laminectomy. Of the five patients who had laminectomies performed for dorsal or lumbar injuries or both, three were improved, one was unimproved and one died of urinary sepsis. Skeletal traction was employed in twenty-four cases of the group presenting cervical dislocation associated with injury to the cord or severe root involvement, and sixteen of these patients died or were unimproved while eight patients showed improvement. In the series, twenty-one patients were treated by orthopedic measures alone.

Statistics on injuries to the cord associated with fracture-dislocation are of little value as a guide to treatment, but a study of the group of eighty cases analyzed in the preparation of this paper corroborates fully an impression we have held for some years, while dealing with a much larger number of cord injuries, that surgery has a limited application in the treatment of such lesions.

#### SUMMARY

1. Laminectomy for injury to the spinal cord due to fracture-dislocation is indicated only for the relief of localized compression of the cord which has not been destroyed at the level of the injury.

2. Compression of the cord can be determined accurately only by the Queckenstedt test. If the test is negative there is no indication for operation in closed injuries, regardless of the severity of the lesion. If the test is positive, laminectomy is indicated only if one believes that the cord possesses some capacity for recovery.

3. Lesions of the cord producing immediate and complete physiologic interruption have, in our experience, shown no indication of recovery regardless of the treatment employed. We have come to regard operation in these cases as a futile procedure.

4. Reduction of the dislocation in the cervical region by skeletal traction, while not improving the patient's chances for restoration of cord function in complete cord lesions, is in such cases useful for the relief of root pains. It is a practical and simple substitute for laminectomy.

5. Severe incomplete cervical cord lesions showing compression with stationary or increasing symptoms may be treated for from eighteen to twenty-four hours by traction. If the symptoms are unchanged and pressure persists after this time, laminectomy under local anesthesia is indicated while traction is being maintained.

6. Severe incomplete lesions of the dorsal region with a block require laminectomy. If there is a compression fracture or fracture-dislocation with a block, laminectomy should precede hyperextension.

7. Prompt laminectomy is indicated in complete lesions of the cauda equina with compression caused by fracture-dislocation.

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### ABSTRACT OF DISCUSSION

DR. FREDERIC C. BOST, San Francisco: It is indeed a privilege to hear from any one who has had as many as 250 cases of spinal injury in a five year period. I think you will all agree with me that such an experience ought to be worth a great deal to all of us. I know of no more serious injury that confronts me as an orthopedist than cervical spine injuries. As soon as one sees a patient with a fracture dislocation of the cervical spine or other portion of the spine, particularly with complete cord injury, one is confronted with a lot of questions. Dr. Coleman and Dr. Meredith in their paper have answered all these questions. It is brought out clearly that the Queckenstedt test, a careful history of the period immediately following injury and a thorough neurologic examination will allow it to be determined whether or not laminectomy is indicated. In the other cases one may resort to skeletal traction. Skeletal traction may be used with the Crutchfield tongs or by any other method which one may desire. One may hope to reduce the fracture-dislocations of the cervical spine without running the danger of doing further damage to the already injured cord. The authors have also brought out clearly the pathologic changes that follow cord injury, and when one realizes what these are one will know that laminectomy can offer but little in a complete cord lesion. We, therefore, as surgeons may follow a policy of nonsurgical intervention rather than subjecting the patient to something that may do him no good. A careful perusal of this paper will show that the principles which it enunciates will allow us to establish a nice regimen on which these patients can be handled.

DR. C. C. COLEMAN, Richmond, Va.: I thank Dr. Bost for his discussion. I should like to correct the erroneous impression he received from my paper as to the number of cases. It is true that we have had 259 cases of spinal injuries in one group of hospitals (Medical College of Virginia) in a five year period, but not 250 cervical injuries as he evidently understood us to say. I am quite sure that he will find the statement in the original paper as to the number of cord injuries as well as the number of spinal injuries in which the cord was not involved.

**The Insulin Molecule.**—Another hormone which evidently has its origin in the amino acids of the blood is insulin. In contrast to thyroglobulin, which yields thyroxine, insulin appears to contain no prosthetic group to which its physiological action may be attributed. Intensive investigations designed to disclose the presence of some peculiar constituent of unusual potency have merely served to emphasize the typical protein nature of the substance. From hydrolysates of the crystalline compound nine amino acids have been separated and identified. These are cystine, tyrosine, glutamic acid, leucine, arginine, histidine, lysine, phenylalanine and proline. Although the above are among the most commonplace components of ordinary proteins, they are said to account for practically the entire insulin molecule. The unique properties of the hormone evidently are due to the structural arrangement of its constituents. In this connection it is of interest to note that many enzymes, particularly those which effect hydrolytic changes, appear to be simple proteins and that their activity is to be ascribed to peculiarities in the disposal of the amino acids within the molecules rather than to the presence of prosthetic groups. According to Northrop, "the formation of enzymes is a special case of the more general problem of the synthesis of proteins."—Rose, William C.: *The Physiology of Amino Acid Metabolism*, *Proc. Inst. Med. Chicago* 12:98 (April 15) 1938.

## SULFANILAMIDE IN THE TREATMENT OF 106 PATIENTS WITH MENINGOCOCCIC INFECTIONS

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The observation of Buttle and his associates<sup>1</sup> that sulfanilamide protected and cured mice of an experimentally induced meningococcic septicemia<sup>2</sup> has been amply confirmed by Proom,<sup>3</sup> Rosenthal and his associates,<sup>4</sup> Levaditi and Vaisman<sup>4</sup> and Brown.<sup>5</sup> Branham and Rosenthal<sup>6</sup> and Brown<sup>5</sup> concluded as a result of their observations on experimental meningococcic infections in mice that a combination of sulfanilamide with an effective antimeningococcus serum produced a greater protective or therapeutic effect than either of the agents by itself. Schwentker, Gelman and Long<sup>6</sup> in a preliminary report considered sulfanilamide to be as effective in the treatment of meningococcic infections in human beings as good specific antisera. All of their eleven patients with but one exception were treated by both the parenteral and the intrathecal route. In this group of eleven patients there was but one death.

Since this report was published, McIntosh and his co-workers,<sup>7</sup> Mitchell and Trachsler,<sup>8</sup> Bernstein,<sup>9</sup> Carey,<sup>10</sup> Basman and Perley<sup>11</sup> and Brennemann<sup>12</sup> have reported that patients ill with meningococcic infections and treated with sulfanilamide have made definite recoveries from their disease. Pongratz<sup>13</sup> has reported recoveries in three patients suffering from meningococcic meningitis who were treated with prontosil<sup>14</sup> parenterally and perorally and with serum by the intrathecal route.

Willien<sup>15</sup> treated five patients ill with meningococcic infection with sulfanilamide. He states that "the clinical response of the patients to treatment with sulfanilamide was satisfactory in every case" and that a favorable outcome was achieved "even with oral administration alone."

Recently Eldahl<sup>16</sup> has reported on the therapeutic use of sulfanilamide in twelve patients suffering from severe forms of meningococcic meningitis. Nine of these patients recovered. All twelve patients were treated by the intramuscular and intrathecal routes. In this paper Eldahl reaches the conclusion that sulfanilamide "has but little effect if the remedy is administered exclusively by mouth or intramuscularly." This statement is in contradiction to the observations of

- From Sydenham Hospital, Baltimore City Health Department.
1. Buttle, G. A. H.; Gray, W. H., and Stephenson, D.: *Lancet* 1: 1286 (June 6) 1936.
  2. Proom, H.: *Lancet* 1: 16 (Jan. 2) 1937.
  3. Rosenthal, S. M.; Bauer, H., and Branham, S. E.: *Pub. Health Rep.* 52: 662 (May 21) 1937. Branham, S. E., and Rosenthal, S. M.: *ibid.* 52: 685 (May 28) 1937.
  4. Levaditi, Constantin, and Vaisman, A.: *Compt. rend. Soc. de biol.* 125: 604, 1937.
  5. Brown, T. M.: *Bull. Johns Hopkins Hosp.* 61: 272 (Oct.) 1937.
  6. Schwentker, F. F.; Gelman, Sidney, and Long, P. H.: *The Treatment of Meningococcic Meningitis with Sulfanilamide*, *J. A. M. A.* 108: 1407 (April 24) 1937.
  7. McIntosh, Rustin; Wilcox, D. A., and Wright, F. H.: *J. Pediat.* 11: 167 (Aug.) 1937.
  8. Mitchell, A. G., and Trachsler, W. H.: *J. Pediat.* 11: 183 (Aug.) 1937.
  9. Bernstein, S. S.: *J. Pediat.* 11: 198 (Aug.) 1937.
  10. Carey, B. W., Jr.: *J. Pediat.* 11: 202 (Aug.) 1937.
  11. Basman, Jack, and Perley, Anne M.: *J. Pediat.* 11: 212 (Aug.) 1937.
  12. Brennemann, Joseph: *J. Pediat.* 11: 238 (Aug.) 1937.
  13. Pongratz, Richard: *Deutsche med. Wchnschr.* 63: 1015 (June 25) 1937.
  14. Prontosil is the disodium salt of 4-sulfamido-phenyl-2'-azo-7'-acetyl-amino-1'-hydroxynaphthalene-3', 6' disulfonic acid.
  15. Willien, L. J.: *Sulfanilamide Therapy in Meningococcic Meningitis*, *J. A. M. A.* 110: 630 (Feb. 26) 1938.
  16. Eldahl, A.: *Lancet* 1: 712 (March 26) 1938.

Marshall and his associates<sup>17</sup> and to those of Long<sup>18</sup> that sulfanilamide easily passes through the normal and inflamed meninges in about the same concentration as is found in the blood.

The present report is complementary to the original communication of Schwentker, Gelman and Long and in it will be discussed the therapeutic results obtained in seventy-two patients ill with meningococcic infections and treated with sulfanilamide alone, and the effects of combined antimeningococcus serum and sulfanilamide therapy in the treatment of thirty-four additional patients suffering from meningococcic infection.

Since the advent of sulfanilamide, 106 patients have received this drug during the treatment of meningococcic infections. For subcutaneous and intrathecal administration, a 1 per cent solution of the powdered sulfanilamide in physiologic solution of sodium chloride

TABLE 1.—*Age Incidence of Patients Treated with Sulfanilamide*

Age, Years.....	0-2	2-5	5-10	10-20	20-30	30-40	40-50	50-60
No. of patients...	12	19	18	22	20	8	3	4

is used. The solution is given intraspinally in amounts 5 cc. less than the quantity of the spinal fluid withdrawn. When given by hypodermoclysis the calculated daily dosage is administered in two divided doses at intervals of twelve hours. Hypodermoclysis is continued twice a day until the patient is able to tolerate sulfanilamide by mouth. I favor the oral administration of sulfanilamide. The drug is given in this manner unless persistent vomiting is present. In comatose patients the tablets are dissolved in water and given by nasal catheter every four hours. In the combined method of therapy serum is injected intraspinally and the same dosage of sulfanilamide given either by mouth or by hypodermoclysis. A minimum of serum is administered in an attempt to reduce the number and severity of serum reactions. I have found that only two intraspinal injections of serum are necessary in the treatment of meningitis and that usually after the first lumbar puncture the spinal fluid is sterile. At the beginning of either method of treatment with sulfanilamide a large initial dose, usually equal to the calculated daily dose, is given either by mouth or by hypodermoclysis.

The first step in the treatment of meningococcic meningitis is lumbar puncture. If the spinal fluid is cloudy and petechiae are found on examination, the treatment of meningococcic meningitis is immediately instituted. If, on the other hand, the diagnosis is doubtful a direct smear of the spinal fluid is first examined and, if gram-negative diplococci are found, the treatment is begun. Serum or sulfanilamide is given intraspinally by the gravity method. Before serum is injected, a sensitivity test to horse serum is done. In the last few cases treated with the combined method, one ampule containing 15 cc. of antimeningococcus serum was injected after drainage of the subarachnoid space. If sulfanilamide alone is used, 5 cc. less than the amount of spinal fluid withdrawn is injected intrathecally. Immediately after the first lumbar puncture, the large initial dose of sulfanilamide is offered. If, for any reason, the patient cannot take the sulfanilamide by mouth, the drug is given by nasal catheter. Only when the patient vomits is the sulfanilamide

given by hypodermoclysis. Hypodermoclysis should be repeated at intervals of not more than twelve hours. The sulfanilamide medication is continued for one week. From twelve to twenty-four hours after the first lumbar puncture a second is done, at which time sulfanilamide or serum is again injected into the subarachnoid space.

I have used the same dosage of sulfanilamide in the combined method as I have in cases in which sulfanilamide alone was given. The daily dose of between 5 and 6 Gm. is rarely exceeded in adults. In infants the dosage is calculated on the basis of 250 mg. per kilogram of body weight daily. In older children the dosage is approximately 1 Gm. to 20 pounds (9 Kg.) of body weight. During the administration of sulfanilamide, fluids are restricted. In adults liquids are limited to between 1,200 and 1,500 cc. a day. The limitation of fluids, I believe, is important in maintaining a therapeutic level of sulfanilamide in the blood and spinal fluid. The state of hydration of the patient is important in determining the extent to which fluids should be limited. In addition, sodium bicarbonate is always given in the same dosage as the sulfanilamide. Acidosis is apt to occur during administration of sulfanilamide, and it is to combat acidosis that sodium bicarbonate is given. Acidosis is especially prone to occur in infants and young children, and it is in this group that the giving of sodium bicarbonate is doubly important.

Among the total number of patients treated with sulfanilamide there were nineteen deaths, a percentage of 18. Seven of the deaths occurred within twenty-four hours. Among the adequately treated patients there were twelve deaths, a case fatality rate of 12 per cent. This figure may be contrasted with a total fatality rate of 27 per cent among 368 patients treated with serum in 1935 and 1936. If the patients who died within twenty-four hours are discounted, 17 per cent of the adequately treated patients who received serum died.

TABLE 2.—*Summary of Results*

Number of Cases	Type of Treatment	Total Deaths		Twenty-Four Hour Deaths		Deaths in Adequately Treated Cases	
		Number	Per Cent	Number	Per Cent	Number	Per Cent
72	Sulfanilamide alone	11	15.27	3	4.16	8	11.59
34	Combined sulfanilamide and serum	8	23.52	4	11.76	4	13.33
106	Sulfanilamide alone and combined sulfanilamide and serum	19	17.92	7	6.6	12	12.12
368	Serum	69	26.9	45	12.12	54	16.71

Sulfanilamide alone was used in seventy-two cases with eleven deaths, a case fatality rate of 15 per cent. There were three deaths occurring within twenty-four hours after hospitalization. When the deaths which occurred within twenty-four hours are deducted, there remain eight patients who died after receiving adequate treatment, or 12 per cent.

The combined method of treatment was instituted in thirty-four cases with eight deaths, a case fatality rate of 24 per cent. In this group there were four deaths which occurred within twenty-four hours, leaving a total of thirty adequately treated cases with four deaths, a fatality rate of 13 per cent. When this

17. Marshall, E. K., Jr.; Emerson, Kendall, Jr., and Cutting, W. C.: *J. Pharmacol. & Exper. Therap.* 61: 196 (Oct.) 1937.  
18. Long, P. H.: Unpublished observations.



method of treatment was first used in Sydenham Hospital, eight patients were treated with four deaths. This method was then discontinued for several months, and since it has been resumed twenty-six cases have been treated with the occurrence of three deaths, two of which occurred within twenty-four hours.

In the group in which the combined method was used there were thirty-two cases in which more than one lumbar puncture was performed. Of this number there was only one case in which more than one positive spinal fluid culture was obtained. At least two lumbar punctures were done on sixty-six of the patients treated with sulfanilamide alone and from eighteen of this number more than one positive spinal fluid culture was obtained. Sixteen of this number had received sulfanilamide by hypodermoclysis throughout or at least for forty-eight hours at the beginning of the treatment. Only two of the eighteen patients had received the drug by mouth. Of those patients receiving sulfanilamide alone, forty-six had been given the drug by hypodermoclysis for at least forty-eight hours at the beginning of treatment and twenty-six were given the drug by mouth. In the group in which the drug was given subcutaneously there were nine deaths, and of those taking sulfanilamide by mouth there were only two. This would seem to indicate that giving the drug by mouth or nasal catheter every four hours was superior to the subcutaneous method of administration every twelve hours.

The concentration of sulfanilamide in the blood and spinal fluid is subject to wide variation when given by hypodermoclysis every twelve hours. At the end of the twelve hour period the sulfanilamide will usually be at a very low level, depending on the urinary output. On the other hand, in cases in which sulfanilamide is given by mouth or nasal catheter every four hours the concentration will tend to be fairly constant at what is thought to be a reasonable therapeutic level.

An attempt has been made to reduce the number of lumbar punctures in the treatment of meningitis. It was found, as already mentioned, that in very few cases was more than one positive spinal fluid culture obtained. I have noted that of all the cases in which sulfanilamide was given by mouth or by gavage every four hours, in only three were there more than one positive spinal fluid culture. Using this factor as a guide, I reduced the number of lumbar punctures, and at present only two are performed. On fifteen patients only three therapeutic lumbar punctures were performed and on fourteen only two were done. Not only does this reduce very markedly the discomfort suffered by the patient in the treatment of meningococcic meningitis but it is also very helpful from the standpoint of the time saved by the hospital attendants. The clinical course of the patient is not altered by the reduction of the lumbar punctures.

Of the total number of patients treated with sulfanilamide, blood cultures were obtained from ninety-four. Thirty-one, or 33 per cent, of this number were positive for the meningococcus. Eighteen blood cultures were obtained from the nineteen patients who died. Ten of the blood cultures obtained were found to be positive for the meningococcus, a percentage of 56.

The complications due to sulfanilamide therapy were relatively mild and infrequent in occurrence. There were three cases of hemolytic anemia and these were treated simply by stopping the drug and forcing fluids. Hemolytic anemia occurred from five days to one week

after sulfanilamide medication was begun and the drug could be discontinued at that time with very little fear of the recurrence of meningococcic infection. There were two cases of sulfanilamide rash, one of which preceded the onset of the hemolytic anemia by twenty-four hours. These cases also occurred at the end of a week, at which time sulfanilamide was usually discontinued. The complications associated with meningococcic infections occurred just as frequently as in the cases in which serum therapy was used. In 368 cases in which serum therapy was used there were ten cases complicated by arthritis and two by endophthalmitis. Among the patients treated with sulfanilamide arthritis developed in five, and endophthalmitis developed in a child who had had a severe injury to the eye two weeks before there had been clinical evidence of the meningococcic infection. There were five cases of deafness occurring in the sulfanilamide treated group and only six in the 368 patients treated with serum. Of the five cases of deafness, in two the deafness was present at the time of admission before treatment was started.

There has been a reduction in the number of recurrences since the introduction of sulfanilamide in the treatment of meningococcic infections. There was only one recurrence in the 106 cases here reported, and in this case sulfanilamide per se was not given but one of the derivatives. On readmission this patient did very well when treated with sulfanilamide alone and recovered very rapidly. Of the 368 serum treated patients there were six recurrences.

#### RESULTS

1. There were 106 patients with meningococcic infection treated at Sydenham Hospital with nineteen deaths, a fatality rate of 18 per cent. The case fatality rate in the adequately treated group was 12 per cent.

2. When sulfanilamide alone was used the fatality rate was 15 per cent. In the adequately treated cases, the fatality rate was 12 per cent.

3. The combined method of treatment was used in thirty-four cases with a case fatality rate of 24 per cent. The fatality rate in the adequately treated group was 13 per cent. Among the last twenty-six patients treated in this manner there were three deaths, two of which occurred within twenty-four hours.

4. The spinal fluid cultures were more consistently sterile after from twelve to twenty-four hours of treatment in those cases in which sulfanilamide was taken every four hours by mouth or by nasal catheter rather than when given every twelve hours by hypodermoclysis.

5. The number of lumbar punctures in the treatment of meningitis has been markedly reduced.

6. The complications due to sulfanilamide therapy were infrequent and very mild. The number of recurrences were reduced. Those complications due to meningococcic infections were not significantly reduced in occurrence.

#### CONCLUSION

Since the introduction of sulfanilamide in the treatment of meningococcic infection there has been a definite decrease in the number of deaths, not only in the adequately treated but also in those fulminating cases which usually terminate fatally within twenty-four hours. The discomfort suffered by the patient directly due to the treatment is lessened owing to the simplification of the treatment, and the hospital stay has been notably reduced.

Harford Road at Herring Run.

COMBINATION COURSES OF BISMUTH  
ADMINISTRATION

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CLEVELAND

Intramuscular bismuth therapy against syphilis ranges from the extreme of very slow absorption from the oil suspensions of compounds that dissolve very slowly in water, such as the subsalicylate, and the other extreme of the relatively rapid absorption from watery solutions. With the watery solutions an effective concentration of bismuth in the blood and tissues is reached

cytate suspensions, adjusted to build up an effective concentration rapidly by use of the watery solution and a continuous concentration meanwhile by use of the salicylate suspension, the injections of the watery solution being graded off as the salicylate concentration rises. The course as projected consisted of ten weekly injections of an oil suspension of bismuth subsalicylate supplemented at the beginning by six injections of a soluble compound, three in the first week, two in the second week, one in the third week and none thereafter.

In one series the subsalicylate was given in the usual weekly dose: 1 cc. of a suspension in olive oil, which contained 0.13 Gm. of bismuth subsalicylate, or 75 mg. of bismuth. In another series double this dose, 2 cc., 0.26 Gm. of bismuth subsalicylate, or 150 mg. of bismuth, was employed. For the water-soluble compounds we chose iodobismitol and sobisminol, because their absorption rate is rapid while their excretion is less

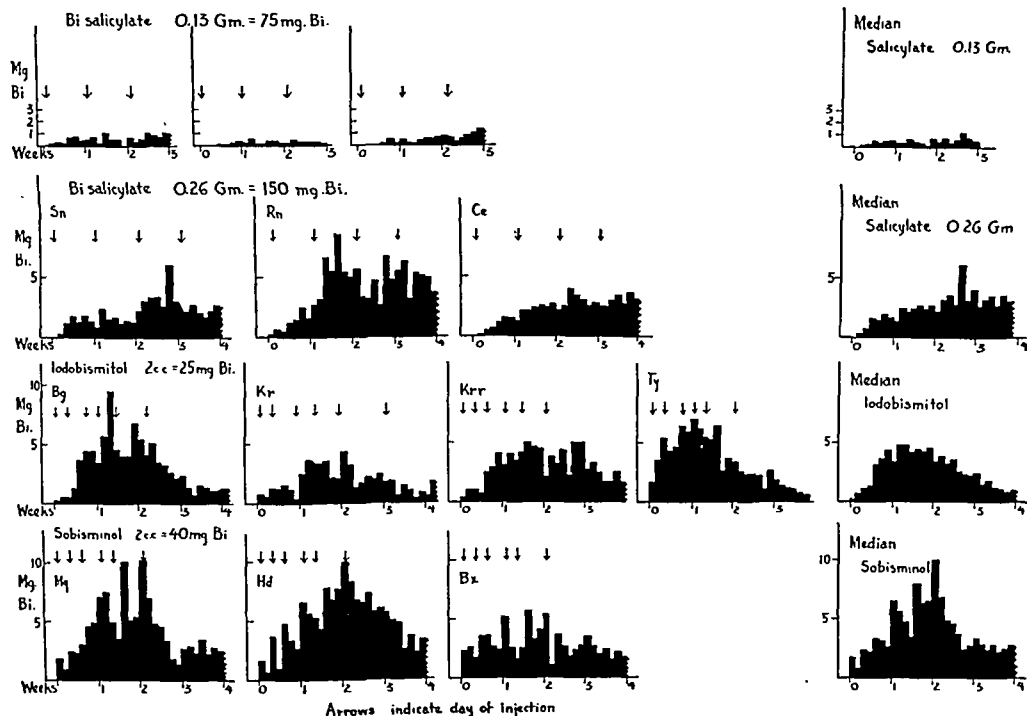


Chart 1.—Daily urinary excretion after injections of (a) bismuth subsalicylate 0.13 Gm., (b) bismuth subsalicylate 0.26 Gm., (c) iodobismitol 2 cc. per injection and (d) sobisminol 2 cc. per injection.

in a short time, perhaps after a single injection. As the excretion of these solutions is also more rapid, their action is relatively brief and they must be administered more frequently. The oil suspensions have the advantage that they may be given at longer intervals. They tend to become cumulative when injected once a week. The effective concentration in the blood is therefore approached more slowly, probably only after from two to four weeks. These extremes are bridged by a variety of bismuth preparations, such as oil suspensions of more soluble compounds and the oil-soluble compounds. It occurred to us that it might be advantageous to approach the problem in a different way, namely by an interlocking sequence of watery solutions and sali-

fugacious than that of the bismuth thioglycollate. The iodobismitol is a solution of 6 per cent sodium iodo-bismuthite and 12 per cent sodium iodide in propylene glycol. The intramuscular dose is 2 cc., equivalent to approximately 25 mg. of bismuth. Sobisminol is a true solution of 3 per cent sodium bismuthate, 8 per cent tri-isopropanolamine and 50 per cent propylene glycol, the remainder being water. The dose used was 2 cc. per injection, 60 mg. of sodium bismuthate, or approximately 40 mg. of bismuth. This resulted in the following experimental courses (the doses being given in milligrams of bismuth for each injection):

1. Bismuth subsalicylate 0.13 Gm., 75 mg. of bismuth
2. Bismuth subsalicylate 0.26 Gm., 150 mg. of bismuth
3. Iodobismitol 2 cc., 25 mg. of bismuth
4. Iodobismitol 2 cc., 25 mg. of bismuth, plus bismuth subsalicylate 0.13 Gm., 75 mg. of bismuth
5. Iodobismitol 2 cc., 25 mg. of bismuth, plus bismuth subsalicylate 0.26 Gm., 150 mg. of bismuth
6. Sobisminol 2 cc., 40 mg. of bismuth

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From the Department of Pharmacology and the Department of Dermatology and Syphilology, Western Reserve University School of Medicine, and City and University hospitals.

7. Sobisminol 2 cc., 40 mg. of bismuth, plus bismuth subsalicylate 0.13 Gm., 75 mg. of bismuth

8. Sobisminol 2 cc., 40 mg. of bismuth, plus bismuth subsalicylate 0.26 Gm., 150 mg. of bismuth

Three or four patients were used for each course, with daily determination of the urinary excretion of bismuth. The curve for each patient is shown in charts 1, 2 and 3, as is the median for each group. For simplicity the median curves were smoothed and projected by extrapolation, for the determinations were not continued after four weeks because of the difficulty of longer hospitalization of patients.

#### IODOBISMITOL AND BISMUTH SUBSALICYLATE

The results are shown in chart 4. The upper set of curves shows (a) the slowly ascending curve when bismuth subsalicylate alone is injected and the dose is 0.13 Gm. (75 mg. of bismuth) weekly. The average

curve reaches a considerably higher level, 2 mg. by the end of the first week and probably 4 mg. in the sixth week. Adding this curve to the curve for iodobismitol (b), which is identical with that in the upper figure, gives the sum shown in the dotted curve, c. This curve ascends gradually to a maximum of 6 mg. at the end of the fourth week and then falls to unite with the salicylate curve at the end of the fifth week, with a level a little above 3 mg. The actual curve runs higher at first, reaching 10 mg. at the end of the second week, and then descends to join the theoretic curve at the sixth week.

#### SOBISMINOL AND BISMUTH SUBSALICYLATE

For sobisminol and bismuth subsalicylate the curves are shown in chart 5, the upper group being for the 0.13 Gm. dose of salicylate (75 mg. of bismuth) and

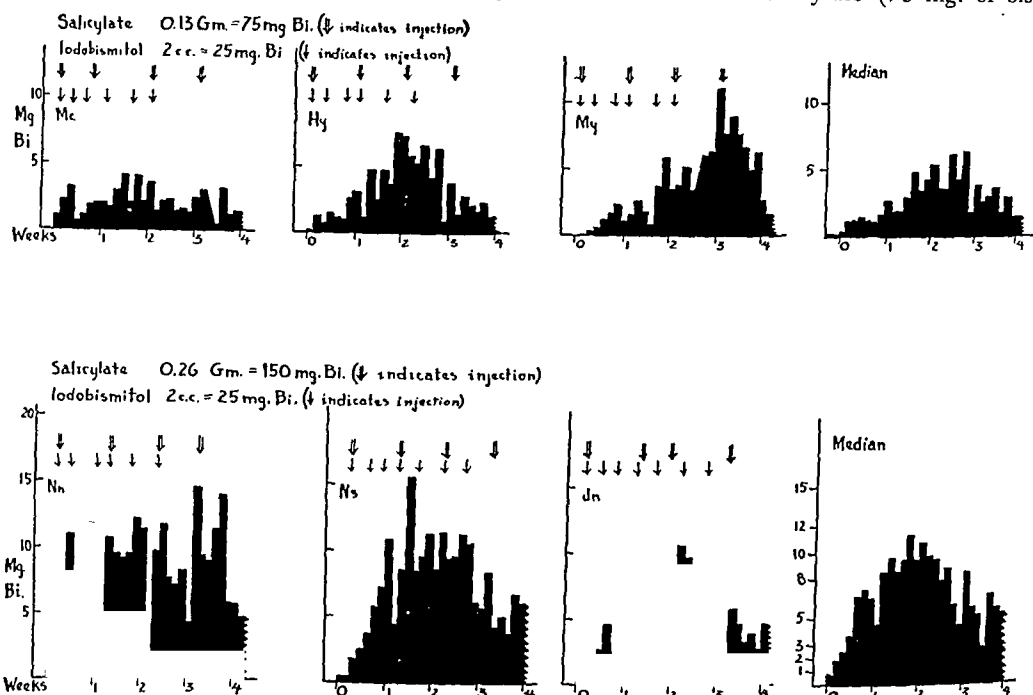


Chart 2.—Daily urinary excretion after injection of iodobismitol plus bismuth subsalicylate 0.13 Gm. and iodobismitol plus bismuth subsalicylate 0.26 Gm.

level of urinary excretion of 1 mg. of bismuth a day is reached in three weeks and 2 mg. of bismuth a day probably in six weeks. With iodobismitol alone (b) by a gradually descending sequence of doses, i. e. three the first week, two the second week, one the third week and none thereafter, the maximum of the excretion curve is reached in about ten days, at 4.5 mg. of bismuth a day. It would have fallen to the 2 mg. level about the end of the third week and below 1 mg. in the fourth week. The sum of the two curves would give the dotted curve (c), which is only slightly higher than the curve for iodobismitol alone for the first two weeks but then falls and keeps practically horizontal at about 2 mg. of bismuth a day until it fuses with the ascending salicylate curve at the seventh week. The actual excretion happens to ascend somewhat more slowly, but to about the same level (5 mg. of bismuth a day), after which its course is practically identical with the arithmetical sum.

The lower set of curves shows (a) the excretion after bismuth subsalicylate 0.26 Gm. (150 mg. of bis-

the lower group for the 0.26 Gm. dose (150 mg. of bismuth). The curves for the subsalicylate are the same as those in chart 4. The curve for sobisminol alone (b), in the descending doses which were used, reaches its maximum at a level of 7 mg. of bismuth about the end of the second week and descends gradually to about 2 mg. at the end of the fourth week and below 1 mg. at the sixth week. The sum of the two curves (c) is but little higher than that of sobisminol alone during the first two weeks, but the descent joins the ascending curve of the salicylate in the sixth week and thus remains above 2 mg. The actual curve for the combined medication (d) is practically identical with the theoretic curve.

When the curve for sobisminol is added to the curve for salicylate in the higher doses, as shown in the lower set of curves (c), the excretion reaches the maximum of 10 mg. of bismuth at the end of two weeks, falls to about 5 mg. by the end of the fourth week and keeps at this level until it joins the ascending curve there at about the end of the seventh week. The actual curve (d) runs somewhat higher.

The variation between the theoretic and the actual observations for the combination are probably not significant. The significant fact is that the combination attained a high excretion level in two weeks, which fell gradually to join the ascending salicylate curve in from five to seven weeks.

With the combination, therefore, the excretion from the very start is materially higher than that which is attained by salicylate alone after from five to seven weeks of administration; namely, 2 mg. of bismuth for the lower dose, 0.13 Gm. (75 mg. of bismuth), and 4 mg. for the higher dose, 0.26 Gm. (150 mg. of bismuth). During the initial two weeks, however, the excretion curve reaches a median of 5 mg. of bismuth with iodobismitol plus salicylate 0.13 Gm., from 6 to 10 mg. with iodobismitol plus salicylate 0.26 Gm., 9 mg. with sobisminol plus salicylate 0.13 Gm. and 12.5 mg.

insoluble bismuth salts, if they have been injected enough times, will reach a therapeutic level in the blood stream. If some combination can be added to this slowly rising bismuth curve that will raise the level within a day or so and hold it long enough so that it may gradually grade off into the rising level from the bismuth subsalicylate, the problem will be solved. This we believe we have achieved by the combined use of iodobismitol or sobisminol and weekly injections of bismuth subsalicylate. The accompanying table illustrates our point.

Such a form of bismuth therapy would be particularly useful in the acute stage of syphilis when the patient is sensitive to arsenic and it is necessary to rely on other antisyphilitic measures. Moreover, for the patient with early syphilis who is just starting therapy, this schema might be employed in the first course of

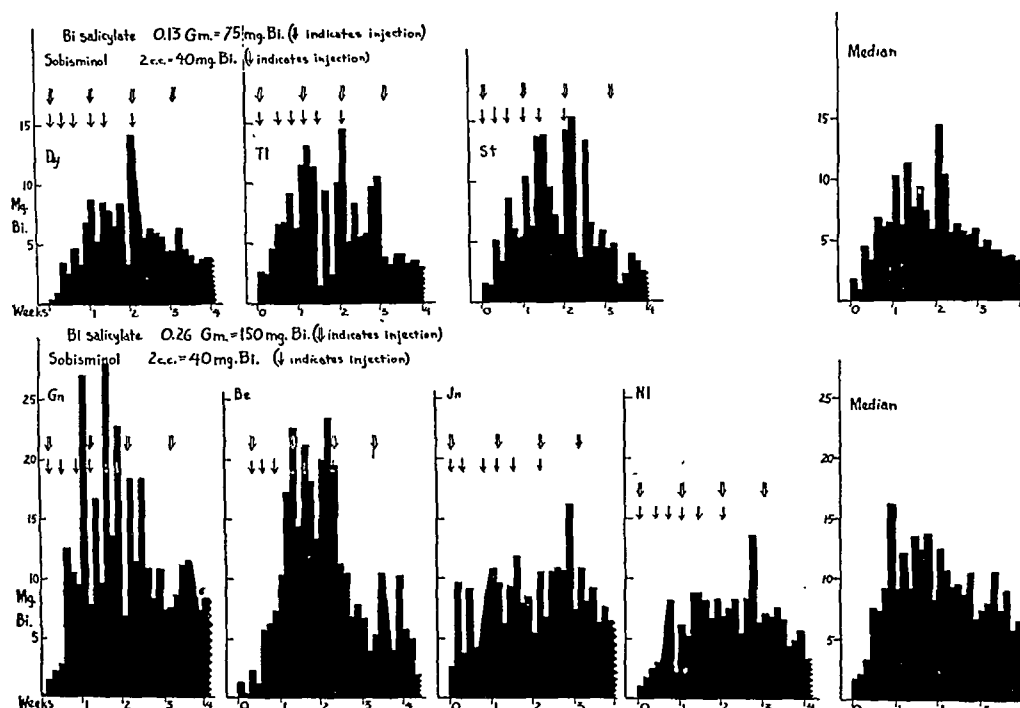


Chart 3.—Daily urinary excretion after injection of sobisminol plus bismuth subsalicylate 0.13 and sobisminol plus bismuth subsalicylate 0.26 Gm.

with sobisminol plus salicylate 0.26 Gm. It is reasonable to assume that this initial intensive medication should be useful for an intensive effect on the spirochetes, which would be maintained when the dose fell to the safer but still effective levels of the ascending salicylate curves. None of the patients showed any toxic effects, nor would these be expected, because the high concentrations are not continued for any length of time. We may add that the 0.26 Gm. dose of salicylate has been used in other cases for the whole course without toxic results.

#### CLINICAL COMMENT

One of the problems with bismuth therapy for syphilis is to achieve a rapid rise of the metal in the blood stream to a therapeutic level and to keep it there without too great hardship on the patient. This can be achieved by biweekly or triweekly intramuscular injections of certain water-soluble bismuth compounds, but what patient will consent to such frequent injection for ten or twelve weeks at a stretch, even if he can afford them? It is well known that eventually certain of the

bismuth therapy when the clinician is desirous of dealing a heavy blow to the spirochetes from another angle than that of arsenic. Again, it would be most useful for the patient who is sensitive to arsenic and has for

#### Schema of Combination Bismuth Treatment

Weeks of Heavy Metal Treatment	
First	X or X <sup>1</sup> plus Y Y Y or Z Z Z
Second	X or X <sup>1</sup> Y Y Z Z
Third	X or X <sup>1</sup> Y Z
Fourth	X or X <sup>1</sup>
Fifth and so forth	X or X <sup>1</sup>

X—bismuth subsalicylate, 1 cc. (0.130 Gm. of bismuth).  
X<sup>1</sup>—bismuth susalicylate, 2 cc. (0.260 Gm. of bismuth).  
Y—iodobismitol, 2 cc. (0.025 Gm. of bismuth).  
Z—sobisminol, 2 cc. (0.040 Gm. of bismuth).

example syphilitic meningitis. In certain cases the clinician would find the bismuth subsalicylate in 1 cc. doses (0.13 of bismuth) sufficient. Certainly for robust males this drug in 2 cc. doses could be employed. With this combined bismuth therapy the somewhat

more irritating injections of water-soluble bismuth preparations would gradually be supplanted by the comparatively painless medication with bismuth subsalicylate.

#### SUMMARY AND CONCLUSIONS

A graded sequence of injections of soluble bismuth preparations (iodobismutol and sobisminol) with continued weekly injections of bismuth salicylate produces a high initial concentration of bismuth as reflected in

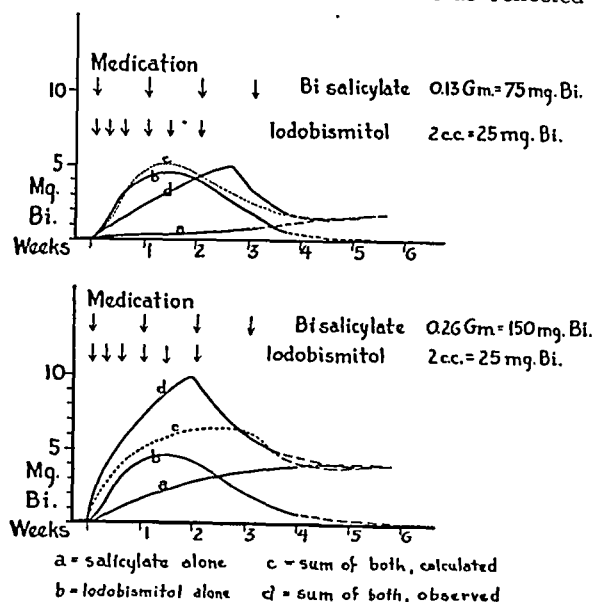


Chart 4.—Median curves for the urinary excretion of bismuth after injection of bismuth subsalicylate (a), iodobismutol (b) and bismuth subsalicylate plus iodobismutol (d). The presumptive further course is indicated by broken lines. The dotted lines (c) represent the arithmetical sum obtained by adding the two curves a and b. The upper set of curves gives results after salicylate 0.13 Gm. and the lower set after salicylate 0.25 Gm.

the urinary excretion, which reaches at the end of two weeks a level of from 4 to 12 mg. of bismuth a day, according to the drugs used. This concentration then falls so as to join the slowly ascending curve characteristic of salicylate injections about the end of from five to seven weeks, so that the median level does not fall below 2 mg. of bismuth for the lower dose (0.13 Gm.) of salicylate and 4 mg. of bismuth for the higher dose (0.26 Gm.) of salicylate. The sequence therefore secures the benefit of the intensive action of the water-soluble bismuth preparations in the early part of the course and the advantages of the convenience of salicylate injections in the latter part of the course.

This form of combined bismuth therapy is offered for use in the treatment of patients with acute syphilis who are sensitive to arsenic when a rapid but prolonged effect of bismuth is called for. It may also be profitably employed as the form of bismuth medication in the treatment of early syphilis.

#### ABSTRACT OF DISCUSSION

DR. GEORGE V. KULCHAR, San Francisco: The paper of Drs. Sollmann and Cole and their associates is a happy compromise, I think, between the two camps existing at present, those who advocate a soluble bismuth compound and those who believe an oil suspended bismuth to be more logical. I think the compromise evoked utilizes the best features of each. When it comes to bismuth, we are somewhat in a state of flux, perhaps induced by several questions. We do not know exactly what we desire therapeutically from a bismuth compound. In other words, is the spirocheticidal effect directly proportional to the absorbed dose, as it would seem from animal experi-

mentation, or should one take the other view, that the bismuth perhaps in combination with some protein acts as a catalyst or a spirochetostatic agent? The second question which leads to indecision is Does urinary excretion truly measure bismuth effect? In other words, is the number of milligrams of bismuth excreted daily in the urine a mathematical expression of the spirocheticidal effect? Another question which causes trouble along the same line is Can bismuth be accurately measured in the blood stream? The order of magnitude of bismuth determinations to a large degree makes the practicing syphilologist wonder whether it is an accurate index of absorption. If the concept is accepted that the spirocheticidal effect is directly proportional to the urinary excretion of bismuth, the method advocated by Dr. Cole and his associates affords rapid approach in the treatment of syphilis, particularly in the cases that they mentioned, and I might add in early syphilis in elderly patients to whom one hesitates sometimes to give an arsphenamine. So far as bismuth salicylate is concerned, this is one means of initiating treatment. The same effect may be obtained by the use of either one of the two soluble compounds mentioned by the authors, sobisminol and iodobismutol. The more rapidly absorbable and consequently excreted compounds seem to me to be more logical. Compounds of this type may be given over long periods of time without cumulative effects on toxicity.

Dr. P. J. HANZLIK, San Francisco: My colleagues at Stanford and Dr. J. R. Scholtz of Los Angeles have sufficient clinical data on bismuth salicylate to indicate that it is inefficient because it is an insoluble and poorly absorbed compound, and the authors' results also show that the absorption is very small. I believe I understand why a bismuth compound of that kind is chosen. It is retained for a long time in the body and assumed there is a continuous bismuth streaming through the tissues for sustained action on the syphilitic virus. But it may be questioned whether there is a continuous, or at least adequate, bismuth streaming through the tissues when one considers the poor absorbability of this product and the local tissue reaction to it. This product is walled off in the muscles and can be found at the injection site for weeks,

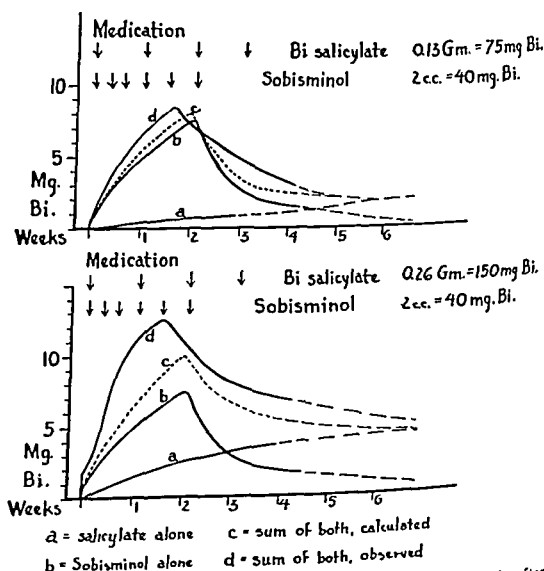


Chart 5.—Median curves for the urinary excretion of bismuth after injection of bismuth subsalicylate (a), sobisminol (b) and bismuth subsalicylate plus sobisminol (d). The presumptive further course is indicated by broken lines. The dotted lines (c) represent the arithmetical sum obtained by adding the two curves a and b. The upper set of curves gives results after salicylate 0.13 Gm. and the lower set after salicylate 0.26 Gm.

months and sometimes even years. Soluble compounds of bismuth are unquestionably superior to the insoluble. I agree with the authors that iodobismutol and sobisminol may be placed somewhere between the most soluble and the least soluble bismuth compounds and produce the desired result so far as the concentration of bismuth and action in the tissues are concerned. The time period for disappearance of the virus

from syphilitic lesions and their healing is inversely proportional to the dosage; in other words, the higher the dosage or the higher the concentration in the tissues, the faster are the clearing and healing of the lesion. The urinary excretion of bismuth is the simplest and most practical guide to the efficiency of medication, much as one would like to have more direct control of the bismuth content of tissues and blood. We have introduced a short clinical method for estimating bismuth in urine, which can be readily applied by an office, technical or clinical assistant. It provides a fairly good chemical control on the treatment. Since insoluble products are much less efficient and desirable, may I suggest the use of an oral bismuth compound, in an exclusive bismuth system, for more efficient and sustained effects and greater convenience? I don't know what the authors think about this, but the oral sobisminol is definitely effective in syphilis. I appreciate the objections to oral medication in the treatment of syphilitic patients, but, aside from the toxicity of arsenicals and mercurials, most of these are not valid and will disappear when there is a better appreciation of the possibilities for bismuth. As for toxicity and possible injuries to viscera, blood and other undesirable effects, sobisminol is not comparable with acetarsone or mercury, whether sobisminol is taken by the patient himself or given under the supervision of a physician.

DR. BEN A. NEWMAN, Los Angeles: It is well known that the most frequent untoward reaction and complaint, especially by patients in private practice, concerns the deposition of bismuth in the gum margins. Have the authors observed any increase in the incidence of gingivitis or stomatitis with this sustained elevation of bismuth in the blood stream?

DR. JOSEPH GRINDON, St. Louis: The advocacy by the authors of the combined use of these two preparations in early syphilis is convincing, but I ask whether in late or latent syphilis, and in the absence of any immediately threatening lesion, it presents any advantage.

DR. HARRY M. ROBINSON, Baltimore: I should like to ask the authors about dermatitis reactions caused by injections of this bismuth compound of 2 decigrams a week. Quite a few cases of dermatitis are found in our clinic. They are of the lichenoid or eczematous types, not exfoliative but still very annoying. I should like to know whether with this high concentration of bismuth the dermatitis is of any more or less frequent occurrence.

DR. ELMORE B. TAUBER, Cincinnati: Before the insoluble preparations of bismuth are relegated to the background and either the oral administrations or the soluble ones are adopted, I want to make a plea for bismuth subsalicylate if it is placed in the proper vehicle. Unfortunately the vehicles that have been placed on the market have been mineral oils and other oils which are the ones when deposited intramuscularly that act as a foreign body and cause a fibrosis with a consequent lowering of the amount of bismuth absorbed. In the last five or six years I have used a preparation of bismuth subsalicylate incorporated in a vegetable compound which is simple, easy to make, with no pain resulting, and this compound is nothing but Crisco, which has stearin in it and which is absorbed easily; and shortly afterward, not within twenty-four to forty-eight hours but within a week, the excretion of from 2 to 3 mg. of bismuth in the urine is observed. It is inexpensive, painless and equal to or better than any preparation that I know on the market. I should also like to ask whether the authors have had any use of oral bismuth.

DR. HAROLD N. COLE, Cleveland: Naturally, one would hesitate to employ dosages of bismuth that would continuously cause an excretion of 15 mg. of metallic bismuth a day in the urine. To Dr. Grindon I will say that this is designed principally for acute syphilis or situations in which a rapid bismuth effect is desired. I do not think it is indicated in late syphilis or for old syphilitic patients but in these acute cases. We have not seen any bad effects from this therapy in the limited number of cases in which we have employed it. Naturally, patients who are getting a dosage of this sort should be watched closely. Probably the first symptom that one would note would be a bismuth line. It is true that once in a while

one encounters a dermatitis from bismuth, but it is uncommon, nothing like the frequency that is encountered with preparations of the arsphenamines that are on the market. With regard to Dr. Tauber's notation about Crisco, a Cincinnati-made product, I would say that we have not used it but that, as he knows, all suspensions of bismuth that are on the market today are in vegetable oils; mineral oils are not employed any more. The reason we are suggesting this type of therapy is that with the water soluble preparations one does get a certain amount of irritation and discomfort, and while it may be justifiable for one or two or three weeks while one is anxious to get them under control, it probably would not be possible to get these patients to continue coming in twice a week for a comparatively irritating preparation as compared to the effects of bismuth subsalicylate. On that account we feel that it would be preferable to change over gradually to this other compound. I should like to say that sobisminol has given the highest excretion of bismuth in the urine of any preparation that we have worked with. We have used this preparation some by mouth in a form that Dr. Hanzlik has worked out. It seems as though from our limited experience there is little or no discomfort from its oral use, and one gets an excretion that compares well with that of iodobismitol. We have had insufficient experience, however, to give any final results on it.

## DIMENSIONS OF THE RED CELLS IN FAMILIAL HEMOLYTIC ANEMIA

WITH PARTICULAR REFERENCE TO  
ATYPICAL CASES

JOSEPH M. HILL, M.D.

DALLAS, TEXAS

Repeated complete measurements of the red cells have been made in seven cases of familial hemolytic anemia studied in Baylor University Hospital during the past two years. The results permit some definite conclusions with regard to the diagnostic value of the size and shape of the erythrocytes (spherocytosis). Furthermore, changes in these dimensions during the course of the disease have been studied in relation to clinical variations, onset of crisis, erythropoiesis and splenectomy. Interpretation of the modifications of corpuscular size and form is based on determination of the normal range of these qualities and consideration of pathologic factors known to affect them.

Alteration of the dimensions of the red cells in familial hemolytic anemia has been recognized almost as long as the disease entity itself. Chauffard<sup>1</sup> in 1907 first noted the decreased diameter, subsequently regarded as the chief characteristic by most writers, including Naegli,<sup>2</sup> Dawson<sup>3</sup> and Haden.<sup>4</sup> Increased thickness and decreased diameter were said by Naegli to be the fundamental inherited feature of the disease. Gänsslen<sup>5</sup> first related this change in shape to increase in fragility. Meulengracht<sup>6</sup> and von Boros<sup>7</sup> expressed

From the Department of Pathology, Hospital Laboratory Division, Baylor University College of Medicine.

Read before the Section on Pathology and Physiology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.

1. Chauffard, M. A.: The Pathogenesis of Congenital Icterus in Adults, *Semana med.* 27: 25, 1907.

2. Naegli, Otto: *Blutkrankheiten und Blutdiagnostik*, ed. 5, Berlin, Julius Springer, 1931, p. 292.

3. Dawson, B. E.: Hume Lectures on Haemolytic Icterus, *Brit. M. J.* 1: 921-928 (May 30) 1931, 963-966 (June 6) 1931.

4. Haden, R. L.: The Mechanism of the Increased Fragility of the Erythrocytes in Congenital Hemolytic Jaundice, *Am. J. M. Sc.* 188: 441-449 (Oct.) 1934.

5. Gänsslen, M.: Ueber hamolytischen Icterus, *deutsches. Arch. f. klin. Med.* 140: 210-226 (Sept.) 1922.

6. Meulengracht, E.: Der chronische hereditäre hämolytische Icterus, *Leipzig, Dr. Werner Klinkhardt*, 1922.

7. von Boros, J.: Ueber gross, Volumen und Form der menschlichen Erythrozyten und deren Zusammenhang: II. Die Merozytose beim hämolytischen Icterus, *Wein. Arch. f. inn. Med.* 12: 255 (Feb.) 1926.



the opinion that spherocytosis is not a specific feature of familial icterus but a regeneration phenomenon unrelated to fragility.

Von Boros<sup>8</sup> and Haden<sup>9</sup> assumed the red cell to be a cylinder for purposes of calculation and expressed the volume-thickness relationship by an index. Haden presented conclusive experimental evidence that there

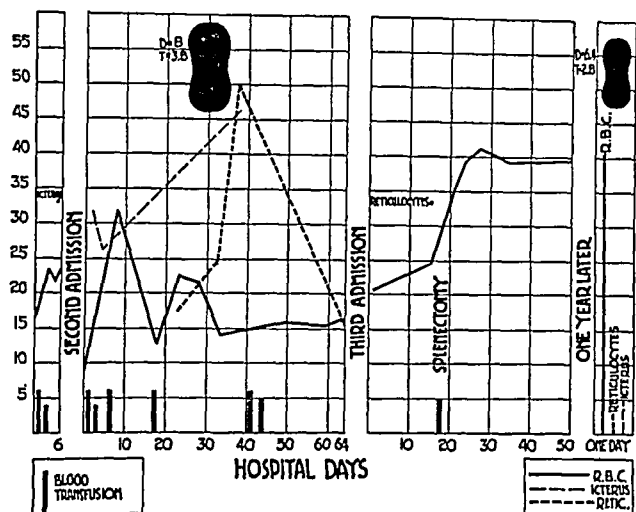


Chart 1.—Progress of the disease in case 1. Read the values for the reticulocytes and the icterus index directly from scale. For the red cell count shift the decimal one place to the left (divide by 10) and read in millions.

is a direct relationship between the degree of approach to sphericity as expressed by this index and the fragility of the red cells and stated that microspherocytosis is the fundamental variation from normal, all other phenomena of the disease being secondary. Castle<sup>10</sup> confirmed this mechanism of fragility and ruled out differences in osmotic behavior as a possible factor. He also devised an absolute rather than a relative index of sphericity, expressing as a percentage the difference between the corpuscular volume and the volume of a sphere of equal surface.

The primary role of the spleen in this disease has been upheld by many hematologists. Doan, Curtis and Wiseman<sup>11</sup> in 1935 recognized spherocytosis but found that the erythrocytes approached the normal form after splenectomy. Vaughan<sup>12</sup> suggested that both erythropoiesis and splenic function are at fault but stated that spherocytosis is not the fundamental abnormality.

Momigliano-Levi and Bairati<sup>13</sup> expressed the opinion that the bone marrow can produce normal cells when relieved of the excessive load of increased destruction in the spleen.

Josephs<sup>14</sup> suggested that an antihemolytic substance normally present to maintain the equilibrium between erythropoiesis and destruction may be absent in sickle cell anemia and hemolytic jaundice.

8. von Boros, J.: Die Behandlung der Anämien, *Ergebn. d. inn. Med. u. Kinderh.* 42: 635-740, 1932.

9. Haden, R. L.: The Volume Thickness Index of the Erythrocyte of Man, *J. Lab. & Clin. Med.* 20: 567-571 (March) 1935.

10. Castle, W. B., and Deland, G. A.: Susceptibility of Mammalian Erythrocytes to Hemolysis with Hypotonic Solutions, *Arch. Int. Med.* 60: 949-966 (Dec.) 1937.

11. Doan, C. A.; Curtis, G. M., and Wiseman, B. K.: The Hemopoietic Equilibrium and Emergency Splenectomy, *J. A. M. A.* 105: 1567-1574 (Nov. 16) 1935.

12. Vaughan, J. M.: Red Cell Characteristics in Acholuric Jaundice, *J. Path. & Bact.* 45: 561-577 (Nov.) 1937.

13. Momigliano-Levi, G. M., and Bairati, A.: "Population in Regard to Diameters and Splenectomized Cases of Hemolytic Icterus: A Study of the Pathogenesis of the Disease, *A. . . .* 1935.

14. Josephs, H. W.: Studies in Hemolytic Anemia. II. The Presence of an Anti-Hemolytic Factor in Human Plasma, *Bull. Johns Hopkins Hosp.* 62: 53-69 (Jan.) 1938.

Since the validity of the results reported in this series of cases depends on the technic employed, a brief statement of method is essential.

#### METHOD

In determining complete dimensions of the erythrocytes, the red cell count, the mean cell diameter and the percentage of packed cells (hematocrit) must be obtained. Simultaneous determination of the hemoglobin is also desirable.

In enumerating the red cells all known precautions with regard to the use of certified equipment, proper shaking and the counting of a large number of cells were observed. Blood was taken from the same sample as that examined with the hematocrit, and 320 small squares were counted.

The mean cell diameter was obtained by a modification of the technic of Price-Jones.<sup>15</sup> The corpuscles were projected at a magnification of exactly 3,000 diameters onto a white target and were measured by fitting to the images circles drawn to a proper scale on white cards. An effective numerical aperture of 1.30 gave full resolution. At least 500 cells were measured in each instance.

For hematocrit determinations Magath tubes were used throughout, and in the later cases duplicate determinations with Wintrobe tubes were also made. Heparin was used as an anticoagulant, but in the duplicates 1.4 per cent sodium oxalate was employed with identical results. All specimens were centrifuged for at least one hour at a minimum speed of 2,500 revolutions a minute. Constant red cell volume was always obtained under these conditions in later experiments. Increasing the speed of centrifugation to 4,500 revolutions showed no significant change in the packing of the red cells.

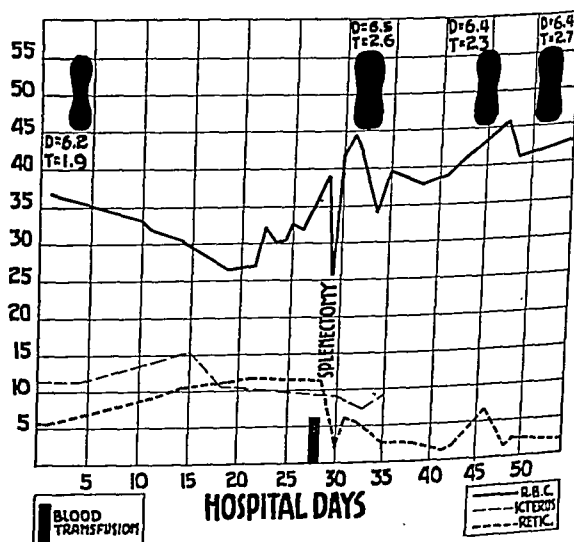


Chart 2.—Progress of the disease in case 2.

Only rarely can all the diagnostic criteria of familial hemolytic anemia be found in one case. In the present study diagnosis was based on several considerations. First, the familial character was considered established if undoubted spherocytosis was found in other members of the family or if a sufficiently definite history of splenomegaly, anemia or jaundice was obtained. Second, the hemolytic character of the anemia was determined

15. Price-Jones, Cecil: *Red Blood Cell Diameters*, New York, Oxford University Press, 1933.

by a study of the state of equilibrium between production and destruction of red cells, indicated by use of laboratory procedures as outlined in the exhibit.<sup>16</sup> Third, repeated measurement of the red cells with the finding of spherocytosis, microcytosis or both on at least one occasion was regarded as most important. Finally, confirmation of the diagnosis was often made

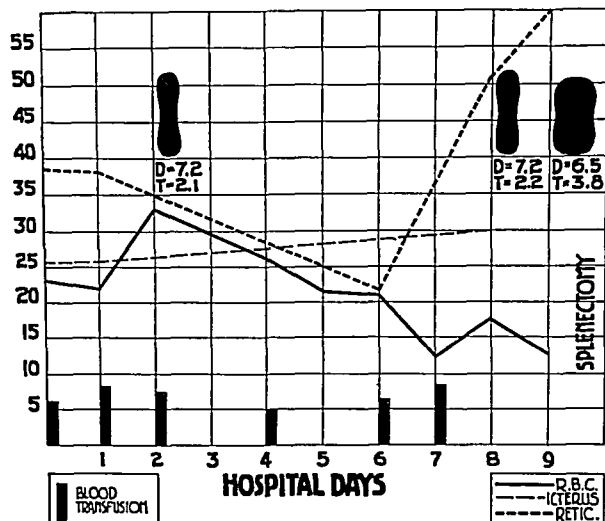


Chart 3.—Progress of the disease in case 3.

possible by examination of the spleen, by the clinical course before and after splenectomy or, in the event of death, by postmortem examination. Studies of the sternal marrow were also employed, particularly in ruling out leukemia.

In expressing corpuscular shape in terms of its approach to spherical form, neither Haden nor Castle reported the limits of physiologic range. Because the biconcave form of the red cell is well adapted to changes in volume and osmotic variations in the blood are known to be accompanied by a shift of water across the red cell membrane, definite alteration in erythro-

TABLE 1.—Measurements of the Red Cells, Case 1\*

Day in Hospital	M.C.V., Cu. Microns	M.C.D., Cu. Microns	M.C.T., Microns	Castle's Index	Haden's Index
30.....	186	8	3.8	36	1.73
1 year later.....	90	6.4	2.8	38.3	1.7

\* Note that the lower the value of Castle's index, the greater the sphericity, whereas in the case of Haden's index the reverse is true. In the tables M.C.V. indicates mean corpuscular volume; M.C.D., mean corpuscular diameter; M.C.T., mean corpuscular thickness; Castle's index, Castle's absolute index of sphericity, and Haden's index, Haden's volume-thickness index.

cytic form must occur. In the first fifteen normal persons of a series now being studied, this variation was borne out. The volume-thickness index ranged from 0.95 to 1.4 with a mean of 1.18, and the absolute index of sphericity varied from 46.4 to 68.6 with a mean of 57.6. The former differs by a significant amount from Haden's normal value of 1, while the latter, because of the greater numerical range, is in practical agreement with Castle's normal value of 59. In addition, similar physiologic variations were found in the same person at different times, for example after exercise.

16. Hill, J. M., and Waters, Lewis: Hematologic Exhibit: IV. The Diagnosis of Hemolytic Anemia, A. M. A. Meeting, San Francisco, June 1938. Scientific Exhibit at the Eighty-Ninth Annual Session of the American Medical Association.

Although Price-Jones, Vaughan and Goddard<sup>17</sup> studied the diameter, volume and thickness of the red cells in 100 normal persons, no calculation of sphericity was made. Their mean diameter of 7.17 microns, however, did not differ significantly from our mean of 7.02 microns. Furthermore, calculation of sphericity from their limits of diameter and volume indicate a possible range as great as ours. Consequently in the series of cases herein reported values above 1.5 for volume-thickness index or below 45 for Castle's absolute index were regarded as definite evidence of spherocytosis.

TABLE 2.—Measurements of the Red Cells, Case 2

Day in Hospital	M.C.V., Cu. Microns	M.C.D., Cu. Microns	M.C.T., Microns	Castle's Index	Haden's Index
4.....	59	6.2	1.9	55.7	1.3
32.....	90	6.5	2.6	41.4	1.6
45.....	75	6.4	2.3	47	1.4
50.....	92	6.4	2.7	38	1.7

Values near the limit of normal were looked on with suspicion, especially with small diameters or marked variation in apparent thickness in the smears.

CASE 1.—K. M., a white boy aged 7, had the acute febrile type of hemolytic anemia, with macrocytosis followed by clinical cure and microcytosis after splenectomy, as illustrated in chart 1. Clinical study showed jaundice, anemia and a palpable spleen. A family history of jaundice was established. The measurements of the red cells are listed in table 1.

CASE 2.—J. T. B., a white boy aged 12, had a moderately severe type of red cell destruction, with clinical features of slight jaundice, splenomegaly, hepatomegaly and an unhealed chronic ulcer of the leg. Hemolytic icterus in his mother was verified by postmortem examination. Chart 2 illustrates the progress of the disease and the response to splenectomy, and table 2 shows the successive dimensions of the red cells.

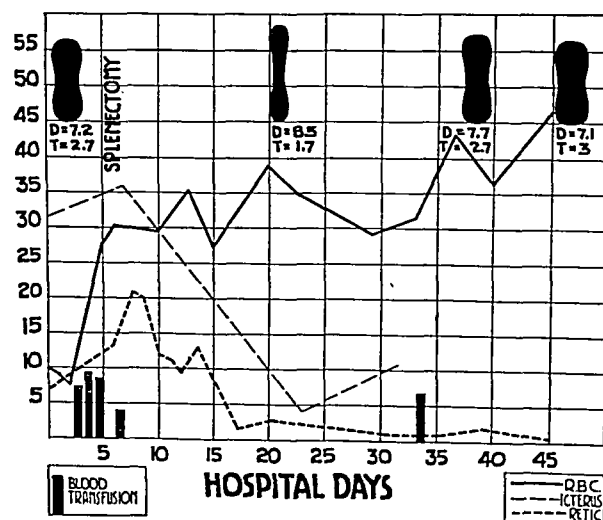


Chart 4.—Progress of the disease in case 4.

CASE 3.—M. C., a white girl aged 14, had an acute hemolytic crisis, as demonstrated in chart 3. No significant family history could be discovered. Clinical study disclosed transient neurologic symptoms, including hemiplegia and paralysis of the left arm. There were pallor, icterus and bleeding gums. The spleen was not palpable. The series of red cell measurements is given in table 3. Death occurred a few hours after splenectomy. Postmortem examination showed peculiar hyaline thrombi in a large number of the smaller vessels of all the sections examined,

17. Price-Jones, Cecil; Vaughan, J. M., and Goddard, H. M.: Normal Hematologic Standards, J. Path. & Bact. 40: 503-519 (May) 1935.

including sections of the heart, brain, liver and spleen. The spleen was otherwise characteristic of familial hemolytic anemia.

CASE 4.—A. T., a white woman aged 54, had slight jaundice, scanty urination, weakness, dyspnea and fever. The spleen was not palpable. A significant family history was demonstrated only through examination of her son's corpuscles. The acuteness of the hemolytic crisis as well as the favorable effect of

again but was refused, and the patient returned home to die two weeks later. The diagnosis was familial hemolytic anemia complicated by cirrhosis of the liver giving a clinical picture identical with Banti's syndrome.

CASE 7.—J. B. A., a white man aged 60, an outpatient, had had intermittent episodes of splenomegaly, anemia and sometimes jaundice since the age of 10. In the five years during which he was under observation, the anemia was only moderate, with the red cell count varying between 3,800,000 and 4,400,000 and the percentage of reticulocytes from 7 to 11. The red corpuscles were constantly microcytic, with an average mean cell

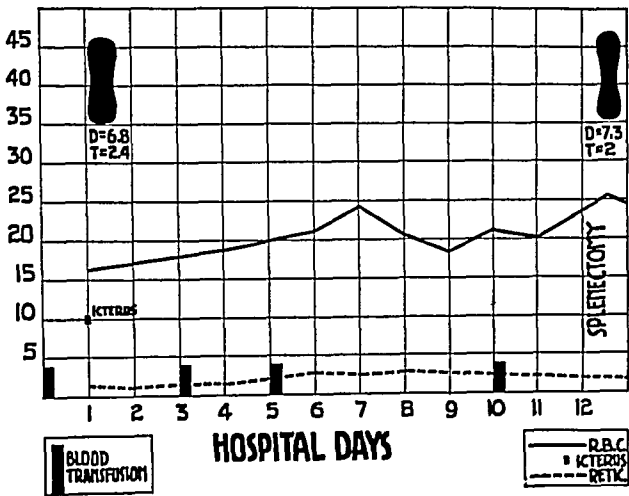


Chart 5.—Progress of the disease in case 5.

splenectomy is easily seen in chart 4. The spleen showed the characteristic enlargement and microscopic picture. The corpuscular dimensions are shown in table 4.

CASE 5.—H. B. W., a white man aged 25, a brother of patient 6, had had previous attacks of anemia, jaundice and splenomegaly. Clinical investigation showed marked enlargement of the spleen and liver, general anasarca and extreme pallor. The results of laboratory tests are given in chart 5 and the complete measurements of the red cells in table 5. The patient refused splenectomy until he felt definitely worse. He died twelve hours after operation. The spleen differed from that in the other cases only in being larger and more heavily loaded with hemosiderin and in showing slight fibrosis. Post-mortem examination showed enlargement of the liver with lobular cirrhosis, bronchopneumonia and early diffuse peritonitis.

CASE 6.—B. M. W., a white youth aged 19, a brother of patient 5, had an identical history and the same clinical appearances. The course of the illness is shown in chart 6. During the first admission, which antedated that of his brother, definite microcytosis and moderate spherocytosis were apparent, as shown

TABLE 3.—Measurements of the Red Cells, Case 3

Day in Hospital	M.C.V., Cu. Microns	M.C.D., Cu. Microns	M.C.T., Microns	Castle's Index	Haden's Index
2.....	89.5	7.2	2.17	59	1.19
8.....	93.4	7.2	2.2	56	1.23
9.....	131	6.55	3.8	28.5	2.33

in table 6. At the second admission, one year later, with the anemia much worse a definite macrocytic tendency was apparent, with abnormal thinness of the red cells. Gastric analysis gave negative results, and leukopenia was present. The white cell count varied from 3,400 to 1,350 during this admission. After failure of transfusion and intramuscular administration of liver extract to arrest his progressive anemia, two doses of 20 cc. of liver extract were given intravenously in an attempt to unmask the possible complicating macrocytic factor of cirrhosis of the liver and to remove any inhibition of erythrocytic maturation. The dramatic response of the reticulocytes, shown in chart 6, was accompanied by progressive reduction in the diameter of the cells, with a slight increase in thickness and fragility but with no improvement of the anemia. Transfusion was of no avail, and the increased destruction of erythrocytes was reflected in the increased icterus index. Splenectomy was recommended

TABLE 4.—Measurements of the Red Cells, Case 4

Day in Hospital	M.C.V., Cu. Microns	M.C.D., Cu. Microns	M.C.T., Microns	Castle's Index	Haden's Index
3.....	110	7.2	2.7	45.3	1.49
20.....	97	8.40	1.7	94	0.81
33.....	128	7.74	2.7	49	1.39
46.....	121	7.12	3	39	1.7

diameter of 6.5 microns. The degree of spherocytosis varied from borderline normal to definitely spheroid. The volume-thickness index varied from 1.4 to 1.9 and Castle's index from 48 to 36. The only atypical feature was the presence of a leukemoid blood picture during the period of observation, with a moderate number of normoblasts, erythroblasts, myelocytes and myeloblasts. The diagnosis was familial hemolytic anemia with ectopic hemopoiesis resulting in a leukemoid blood picture.

COMMENT

The finding of considerable variation in the volume-thickness relationship of normal red cells, as expressed by Haden's or Castle's method, is by no means an exception to the usual biologic rule. Furthermore, such variation is probably an expression of functional changes in the corpuscles of an individual as well as a normal morphologic difference between individuals. It is also in complete harmony with the limits of normal established for cell volume and diameter.

Apparently this series of cases represents the first determination of the range of the indexes of Castle and Haden. A comparable variation in thickness of

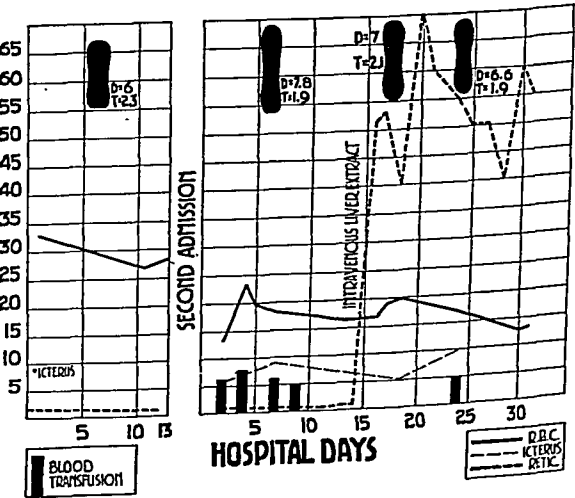


Chart 6.—Progress of the disease in case 6.

the red cells has already been reported by Price-Jones, Vaughan and Goddard, in which they found no correlation with the diameter. Unfortunately, no calculation of sphericity was made.

The interpretation of values for erythrocytic sphericity must be made with due regard to the normal limits as well as to possible physiologic variations in

the individual case. Many values previously reported as indicative of spherocytosis were undoubtedly within the normal range.

In the present series of cases the effect of physiologic changes probably accounted for a large measure of the variations seen. However, there was an undoubted general tendency to spherocytosis, since in every case but one there was at least one occasion when definite spherocytosis occurred. From this it is evident that only repeated examinations are of diagnostic significance unless values well beyond the normal range are obtained.

Decrease in the diameter of the erythrocytes appeared to be even more constant. In addition, a fairly definite relationship to spherocytosis was evident. As a rule, the thickest cells had the smallest diameters.

The one notable exception to microcytosis occurred in the fairly typical case 1. In this case a definitely macrocytic spherocytic corpuscle of enormous volume was seen in the first examination. The mechanism of production of this atypical variety of cell is not well understood. However, the explanation of Davidson

TABLE 5.—Measurements of the Red Cells, Case 5

Day in Hospital	M.C.V., Cu. Microns	M.C.D., Cu. Microns	M.C.T., Microns	Castle's Index	Haden's Index
2.....	86	6.8	2.4	45.6	1.4
13.....	81	7.3	2	65.3	1.05

TABLE 6.—Measurements of the Red Cells, Case 6

Day in Hospital	M.C.V., Cu. Microns	M.C.D., Cu. Microns	M.C.T., Microns	Castle's Index	Haden's Index
6 1st admission.....	71	6	2.5	40	1.64
6 2d admission.....	90	7.8	1.88	76.3	0.97
17.....	81	7	2.1	58.9	1.2
24.....	66	6.6	1.92	60.8	1.16

and Fullerton<sup>18</sup> is probably the most satisfactory, according to which megaloblastic transformation of the marrow is assumed as a result of hyper-regeneration. A rather prolonged hemolytic crisis of relatively severe degree, as seen in case 1, is apparently the stimulus to this type of response.

Another complicating factor must be considered in the diagnosis in rare atypical cases, namely coincident pathologic processes which tend to result in the formation of abnormally thin or abnormally large red cells. For example, cirrhosis of the liver exhibits both of these tendencies. Cases 5 and 6 evidently represent slightly different degrees of this type of complication. When studied together, the cases of these two brothers present conclusive evidence of two conditions tending to produce anemia but mutually opposed in their effect on corpuscular size and shape. In case 5 postmortem examination showed cirrhosis of the liver, while in case 6 the effect of liver therapy was definitely indicative of a similar mechanism. In addition, the unmasking of microcytosis corroborates the diagnosis of familial hemolytic anemia.

Finally, this study fails to reveal any correlation between the degree of spherocytosis and the severity of the disease. Neither was a definite relationship established between spheroid form and the onset of crisis, the rapidity of regeneration of the red cells or even the effect of splenectomy.

## SUMMARY AND CONCLUSIONS

Microcytosis was found on at least one occasion in six of seven cases of familial hemolytic anemia, while spherocytosis was found in five cases.

Spherocytosis may be absent in the presence of complicating factors such as cirrhosis of the liver.

Macrocytosis was observed in one case during crisis.

No significant correlation could be established between spherocytosis and the severity of the disease, onset of crisis, rapidity of regeneration of the red cells or effect of splenectomy.

## ABSTRACT OF DISCUSSION

DR. RUSSELL L. HADEN, Cleveland: Dr. Hill has verified the observation that the increased tendency to hemolysis of red cells in congenital hemolytic jaundice is dependent on the spherocytic shape of the cell. I have recently studied a patient, however, who had the typical clinical picture of congenital hemolytic jaundice and spherocytosis of the red cells without increased fragility. I cannot explain this observation. Several factors influence the shape of the cell in congenital hemolytic jaundice. The simultaneous occurrence of an iron deficiency will flatten the spherocyte. If a deficiency in the erythrocyte-maturing factor supplied by liver occurs, the cell becomes larger. If a patient has anemia with cells of very small diameter, the disease is usually congenital hemolytic icterus and should be treated by splenectomy. On the other hand, hemolytic anemia with cells of large diameter should seldom be treated surgically. Dameshek has shown recently that under certain conditions, such as infection, the shape of the cell may change so that at times it is sufficiently spherocytic to be more fragile than normal. Thus the spherocytosis does not depend on heredity alone.

DR. M. C. RIDDLE, Portland, Ore.: Dr. Hill's paper points out that one cannot be too complacent in one's fixed ideas on the hemologic pictures of the various disorders discussed. It is extremely important that the clinical features of these diseases should be taken into account as well as the laboratory features. I have under observation a patient with familial jaundice which illustrates the features discussed. This patient has passed through three phases so far as the hemologic picture is concerned. In the first phase the typical hemologic picture of familial jaundice was present. Then there developed a leukemoid picture with a white count in the vicinity of 40,000, with considerable numbers of immature myeloid cells. In the third phase leukopenia and pronounced macrocytosis developed. The blood film was indistinguishable from that of pernicious anemia. This macrocytosis responded to the use of liver extract. I accounted for this response in much the manner in which Dr. Haden accounted for the macrocytosis discussed by Dr. Hill.

DR. JOSEPH M. HILL, Dallas, Texas: The time available did not permit a discussion of fragility. It is well known that undoubted hemolytic anemia may not be accompanied by increased fragility. This can be explained by the absence of spherocytosis at least during certain phases. I did find a rather definite relation between spherocytosis and fragility; in fact, it was more definite than the relation of clinical features and spheroid red cells. I believe that the use of liver therapy for this type of anemia is rational, since depletion of the stored erythrocyte-maturing factor apparently can result from prolonged excessive demand incident to increased erythropoiesis. This situation is apt to occur when the disease is unrecognized and untreated and there is damage to the liver. With regard to the leukemoid blood picture associated with this disease, there are probably two types: first, the acute crisis representing an outpouring of cells from the bone marrow and, second, the type that occurred in case 7. I believe that in this instance, with a compensated form of hemolytic jaundice, ectopic hemopoiesis resulted in lack of normal control of blood cell output. It may be difficult in such cases to differentiate the disease from myelogenous leukemia. The patient has been followed for five years, and I feel certain that he does not have leukemia, although at one time he was treated for it.

18. Davidson, L. S. P., and Fullerton, H. W.: Some Rare Types of Macrocytic Anemia, *Quart. J. Med.* 7: 43-54 (Jan.) 1938.

## THE OUTLOOK IN THROMBO-ANGIITIS OBLITERANS

BAYARD T. HORTON, M.D.  
ROCHESTER, MINN.

In the past decade I frequently have had anxious patients with thrombo-angiitis obliterans ask the question What is the outlook in my case? Hence the title of this paper. In an attempt to answer the question in such a manner that it may be of some service both to patients and to fellow workers in the field, I have carefully reviewed all the cases of thrombo-angiitis obliterans that have been observed at the Mayo Clinic from 1907 to 1937 inclusive. I have myself observed and studied a large number of these cases.

The past decade has witnessed marked changes in the attitude of physicians toward thrombo-angiitis obliterans largely because of a better understanding of the disease. Prior to this time the diagnosis of thrombo-

20 and 50 years. In spite of the fact that it was formerly supposed to occur almost exclusively among Jews, it is now known to affect persons of all races. The cause of the disease has not been established. Its usual course is rather slow. As a rule the main vessels of the feet and legs are involved early, those in the upper extremities later.

The disease is characterized by a chronic relapsing lesion of the vessels in which the occlusive process and the development of collateral circulation struggle for supremacy. The element of time is most important in this struggle, since on it rests the preservation of the parts. If the intervals between relapses are short and the time for the development of collateral circulation is inadequate, trophic changes and gangrene are likely to ensue. Conversely, if the intervals between relapses are long, the collateral circulation becomes adequate and a sufficient supply of blood to the distal parts is assured. The first consideration regarding prognosis is therefore the frequency of exacerbations of the disease. Experience in a large number of cases shows clearly that the belief that amputation invariably will be necessary is not justified.

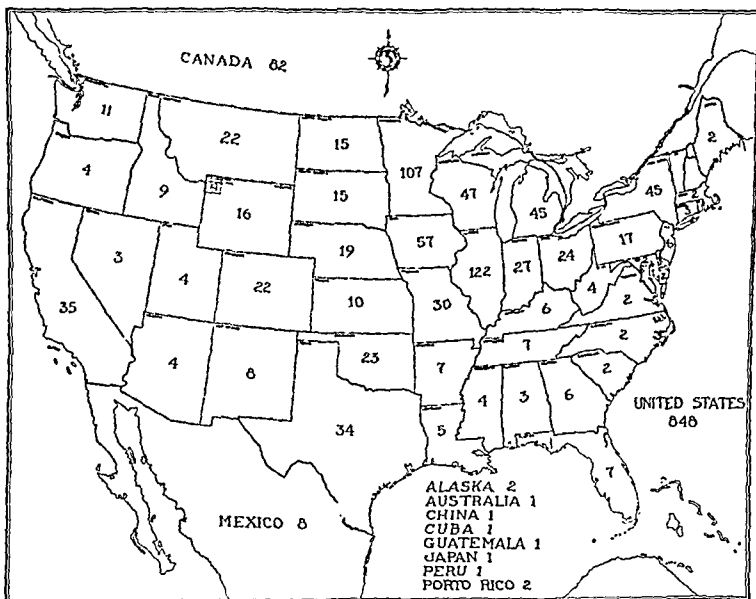


Fig. 1.—Geographic distribution of cases of thrombo-angiitis obliterans.

angiitis obliterans carried with it the implication that amputation of one or both lower extremities would follow inevitably and, once the diagnosis had been established, it was suggested that amputation of the involved extremity be carried out promptly. For example Buerger,<sup>1</sup> in his book published in 1924, said that "amputation just above the middle of the leg" was performed in one case "because the little toe looked as though it was going to die off." At the clinic we have become more optimistic from year to year regarding the disease, and we feel that, if the diagnosis is made early and if the patient follows the thorough instructions which are given regarding the care of his extremities, he stands a good chance of continuing to walk on two feet throughout life.

Thrombo-angiitis obliterans is a chronic occlusive arterial disease involving chiefly the extremities and affecting, for the most part, men between the ages of

### BASIS OF PRESENT STUDY

In the thirty-one years from 1907 to 1937 inclusive, 1,374 patients with thrombo-angiitis obliterans registered at the clinic. But since 426 of these patients registered more than once during this period, and some of them as many as ten times, the present study will be confined to the 948 individual patients represented (table 1). Throughout this report considerable material will be presented which bears on the old question of the relative susceptibility to this disease manifested by males and females and by Jews and Gentiles.

### GEOGRAPHIC DISTRIBUTION

The patients in this series came from every state in the Union except Rhode Island, Vermont and New Hampshire; in addition there were patients from Canada, Mexico, Alaska, Australia, China, Cuba, Guatemala, Japan, Peru and Porto Rico (fig. 1). They came from practically every walk of life. The same fundamental pathologic process was present in all cases and the signs and symptoms, as well as the clinical course, were strikingly similar. It is interesting to note that, while in the majority of cases of thrombo-angiitis obliterans the symptoms begin during the winter months, in this study the incidence of amputations in the warmer sections of the country, such as Florida and California, was as high as that observed in Minnesota and Canada (fig. 2). Therefore, in spite of the fact that patients went to live in warm sections of the country after having been observed at the clinic, amputations were still necessary. The explanation of this probably is that vasospasm in the collateral circulation does not disappear until the environmental temperature is 82 F. or above, as our studies at the clinic have proved. It is difficult to find in the United States a place where such a temperature is maintained.

### AGE, SEX AND RACE

The distribution by age and sex is represented in table 2. The mean age of all patients was 41.8 years. More than 70 per cent of the 948 patients were in the

From the Division of Medicine, the Mayo Clinic.  
Read before the Section on Practice of Medicine at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.  
1. Buerger, quoted by Samuels, S. S.: *The Diagnosis and Treatment of Diseases of the Peripheral Arteries*, New York, Oxford University Press, 1936, p. 73.

third and fourth decades of life, the ages for the entire series varying from 17 to 73 years. The sex incidence is likewise of interest. Of the 948 patients twenty-one were women, which indicates an incidence of approximately 98 per cent in men.

I know of no other disease in which such common tissues as the veins and arteries are involved that is so exclusively confined to one sex as is thrombo-angiitis obliterans. No adequate explanation has yet been brought forth to account for this most unusual sex distribution. Too few cases of thrombo-angiitis obliterans have thus far been observed in women for one to compare adequately the severity of the disease as it affects them with its severity in the case of men. I have been under the impression that the disease runs a milder course in women than in men, but more cases will have to be observed for a longer period before conclusions in this respect can be drawn.

Of the twenty-one women patients, five were Jewish and sixteen were Gentiles. Of the 927 men, 257 were Jews and 670 were Gentiles. Thus roughly 28 per cent of the 948 patients were Jews and 72 per cent were Gentiles. In earlier reports<sup>2</sup> from the clinic, 55 per cent of the patients were Jews and 45 per cent were Gentiles. Thus far we have not observed thrombo-angiitis obliterans affecting a full-blooded Negro, although such cases have been observed elsewhere; one of our patients was, however, part Negro. More than twenty-eight different nationalities were represented in this series.

#### RACE AND DEGREE OF SMOKING

If a patient smoked five cigarettes a day he was listed as a grade 1 smoker, if ten cigarettes a day as a grade 2 smoker, if fifteen cigarettes a day as a grade 3 smoker and if twenty cigarettes or more a day as a grade 4 smoker (table 3). Many of the grade 4 smokers used as many as sixty cigarettes a day. One patient, for example, smoked at least twenty cigarettes before breakfast. Of the total of 948 patients who had thrombo-angiitis obliterans, 93 per cent were cigarette smokers; in 66 per cent of the cases the degree of smoking was graded 3 or 4.

Of the 262 Jews, 238 were smokers (table 3). Sixty-five of them were grade 1 or grade 2 smokers, and of these twenty-five, or 38 per cent, underwent amputation. Of the 173 grade 3 or grade 4 smokers fifty-eight, or 33 per cent, were subjected to amputation. Thus of the 238 Jewish patients who had thrombo-angiitis obliterans and who smoked, eighty-three, or 35 per cent, underwent amputation, whereas only 21 per cent of the nonsmokers were subjected to amputation. This report includes amputations elsewhere as well as at the clinic.

Of the 686 Gentile patients, 642 were smokers. Ninety of the 189 grade 1 or grade 2 smokers (48 per cent) were subjected to amputation; of the 453 grade 3 or grade 4 smokers 207 (46 per cent) underwent amputation. Of the forty-four Gentile patients who were nonsmokers sixteen, or 36.4 per cent, underwent amputation. Thus of all Gentiles who smoked

297, or 46 per cent, underwent amputation, whereas only 36.4 per cent of the nonsmokers were subjected to amputation.

It has been accepted generally that thrombo-angiitis obliterans is somewhat more severe among the Jews than among representatives of other races. This does not seem to be borne out by the present studies. Of the 262 Jews 33.6 per cent underwent amputation, whereas of the 686 Gentiles 45.6 per cent were subjected to amputation (table 3). These figures are for both sexes and for amputation performed both at the clinic and elsewhere.

The present study tends to indicate, however, that amputations were less frequent among nonsmokers. It has been difficult to persuade patients with thrombo-angiitis obliterans to stop smoking. In the past ten years numerous experimental studies have been reported in the American literature, which establish rather definitely that the use of tobacco does produce some vasospastic effects. Lampson,<sup>3</sup> Maddock and his

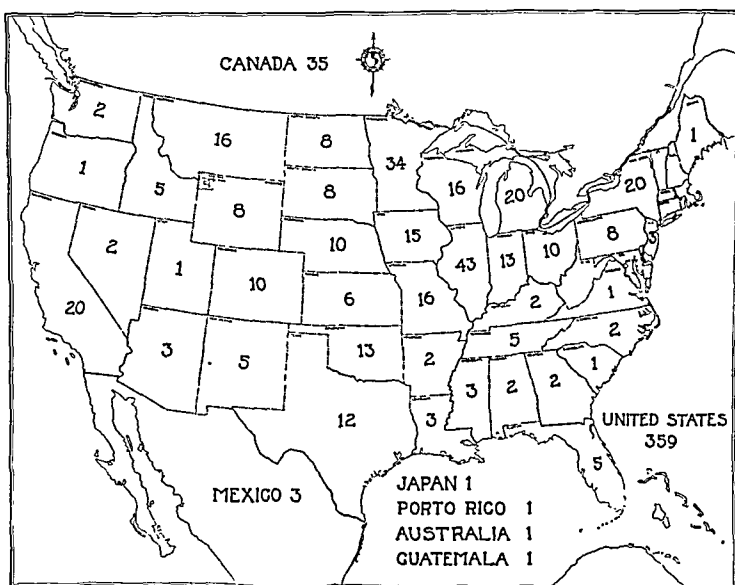


Fig. 2.—Geographic distribution according to amputations.

co-workers,<sup>4</sup> Barker<sup>5</sup> at the Mayo Clinic, as well as Wright and Moffat<sup>6</sup> and Johnson,<sup>7</sup> have contributed important articles from this standpoint. Haggard and Greenberg<sup>8</sup> noted a definite elevation of the blood sugar following the use of tobacco. They were of the opinion that the mild hyperglycemic effect, as well as the effect on the blood pressure, might be a secondary result of the adrenal stimulation which is brought about by the action of nicotine on the sympathetic nerves and which results in an increased secretion of epinephrine. Herrell<sup>9</sup> recently has reported the case of a man, aged 57,

3. Lampson, R. S.: A Quantitative Study of the Vasoconstriction Induced by Smoking, *J. A. M. A.* **104**: 1963-1966 (June 1) 1935.

4. Maddock, W. G.; Malcolm, R. L., and Coller, F. A.: Thrombo-Angiitis Obliterans and Tobacco: The Influence of Sex, Race and Skin Sensitivity to Tobacco on Cardiovascular Responses to Smoking, *Am. Heart J.* **12**: 46-52 (July) 1936.

5. Barker, N. W.: Vasoconstrictor Effects of Tobacco Smoking, *Proc. Staff Meet., Mayo Clin.* **8**: 284-287 (May 10) 1933.

6. Wright, I. S., and Moffat, Dean: The Effects of Tobacco on the Peripheral Vascular System; Further Studies, *J. A. M. A.* **103**: 318-323 (Aug. 4) 1934.

7. Johnson, H. J., and Short, J. J.: Effect of Smoking on the Skin Temperature, *J. Lab. & Clin. Med.* **19**: 962-966 (June) 1934.

8. Haggard, H. W., and Greenberg, L. A.: The Effects of Cigarette Smoking upon the Blood Sugar, *Science* **79**: 165-166 (Feb. 16) 1934.

9. Herrell, W. E., and Cusick, P. L.: Vascular and Retinal Abnormalities Following Inhalation of Tobacco Smoke: Preliminary Report, *Proc. Staff Meet., Mayo Clin.* **13**: 273-279 (May 4) 1938.



whose systolic and diastolic blood pressure invariably became markedly elevated and whose retinal arteries became constricted following the smoking of a cigaret.

AMPUTATIONS

It will be noted in table 1 and in figure 3 that according to the total registrations 15.6 per cent of the patients underwent amputation at the clinic. One hundred and seventy-eight of the patients were subjected to one or more amputations at the clinic, the total number of amputations performed being 214. Six of these patients were women, 172 were men. No amputations for thrombo-angiitis obliterans were carried out at the clinic from 1907 to 1916 inclusive, and the percentage of amputations from 1928 to 1937 inclusive was definitely less than during the previous ten years. Later in this report it will become evident from the statistics concerning amputation that progress has been made in the nonsurgical management of this disease.

*Major and Minor Amputations.*—In this study the loss of a finger or a toe was considered to constitute a minor amputation; the loss of a foot, a leg or a hand was considered a major amputation. Eighty-eight Jews and 313 Gentiles underwent amputation. The percentage of each of these two racial groups who were subjected respectively to major and to minor amputa-

TABLE 1.—Thrombo-Angiitis Obliterans (1907-1937 Inclusive):  
Distribution of Cases and Incidence of Amputations

Year	Total Regis- trations of Patients with Thrombo-Angiitis Obliterans	New Cases		Amputations*	
		Number	Per Cent of Regis- trations	Number	Per Cent of Regis- trations
1937.....	73	39	53.4	5	6.8
1936.....	91	55	60.4	15	16.5
1935.....	98	61	62.2	23	23.5
1934.....	97	52	53.6	10	10.3
1933.....	101	57	56.4	15	14.8
1932.....	107	74	69.2	17	15.9
1931.....	108	64	59.2	16	14.8
1930.....	136	104	76.5	21	15.4
1929.....	113	91	80.5	7	6.2
1928.....	86	64	74.4	15	17.4
1927.....	62	40	79.0	14	22.6
1926.....	67	51	76.1	9	13.4
1925.....	47	39	83.0	8	17.0
1924.....	39	27	69.2	10	25.6
1923.....	33	29	87.9	4	12.1
1922.....	25	23	92.0	7	28.0
1921.....	22	18	81.8	7	31.8
1920.....	12	10	83.3	2	16.7
1919.....	16	13	81.2	4	25.0
1918.....	12	9	75.0	2	16.7
1917.....	12	10	83.3	2	16.7
1916.....	6	3	50.0	..	....
1915.....	5	4	80.0	..	....
1914.....	1	..	....	..	....
1913.....	1	..	....	..	....
1912.....	0	..	....	..	....
1911.....	1	..	....	..	....
1910.....	1	..	....	..	....
1909.....	1	1	100.0	..	....
1908.....	0	..	....	1	100.0
1907.....	1	1	100.0	..	....
Total.....	1,374	948	69.0	214	15.6

\* At the clinic.

tion is given in table 3. Of the total of 401 patients who underwent amputation 276, or 69 per cent, underwent major amputations; the remaining 31 per cent had minor amputations (table 3).

Seventy-one per cent of all amputations at the clinic for thrombo-angiitis obliterans from 1918 to 1927 inclusive were major amputations, whereas only 63 per cent of all amputations from 1928 to 1937 inclusive were major amputations. It is still more encouraging to note that during the past five years (1933-1937)

only 48 per cent of amputations at the clinic were of the major type. This indicates definite progress in the medical and surgical management of this disease.

*Amputations at Three, Five and Ten Year Periods After the Onset of the Disease.*—In this phase of the study patients were divided into three, five and ten year groups, each group indicating the period of time which had elapsed since the onset of the condition. Thus of

TABLE 2.—Thrombo-Angiitis Obliterans (1907-1937 Inclusive):  
Age and Sex Distribution

Age, Years	Males		Females		Total	
	Num- ber	Per Cent	Num- ber	Per Cent	Num- ber	Per Cent
10-19.....	2	0.2	..	....	2	0.2
20-29.....	84	9.1	4	19.0	88	9.3
30-39.....	302	32.6	7	33.3	309	32.6
40-49.....	375	40.4	9	42.9	384	40.5
50-59.....	148	16.0	..	....	148	15.6
60-69.....	14	1.5	1	4.8	15	1.6
70-79.....	2	0.2	..	....	2	0.2
Total.....	927	100.0	21	100.0	948	100.0
Mean age, years.....	41.8		38.8		41.8	
Per cent.....	97.8		2.2		100.0	

the 828 subjects in the three year group 694 (84 per cent) were followed for a period of three years from the onset of thrombo-angiitis obliterans. Of these 694, 215 (31 per cent) were subjected to amputation (table 4). This would indicate that approximately 70 per cent of patients who have thrombo-angiitis obliterans will go for three years after the onset of the disease without amputation being necessary. In the five year group 628 (80 per cent) of the 785 patients were traced and, of these, 248 (39.5 per cent) underwent amputations. This in turn would indicate that approximately 60 per cent of patients who have thrombo-angiitis obliterans will go for five years without the necessity of amputation. In the ten year group 334 (77 per cent) of the 433 patients were traced, and of these 59.9 per cent had amputations. This would indicate that approximately 40 per cent of patients who have thrombo-angiitis obliterans will go for ten years after the onset of the disease without amputation. These figures perhaps give a better insight into the outlook in thrombo-angiitis obliterans than anything else.

*Bilateral Major Amputations.*—Of the 948 patients, eighty-five underwent bilateral amputation of the legs; sixteen of these patients were Jews and sixty-nine were Gentiles. Eleven bilateral amputations were carried out at the clinic, all of the patients being Gentiles. Thirty-five per cent of these eighty-five patients who underwent bilateral amputations live in warm climates. Eighteen of the eighty-five are dead. At the clinic we have never had to amputate a hand because of thrombo-angiitis obliterans, but in this series of cases the hand of one subject had been amputated prior to his admission to the clinic; the hand of a second patient and both hands as well as both legs of a third patient were amputated after the patients left the clinic.

PHYSICIANS WITH THROMBO-ANGIITIS OBLITERANS

Twenty-two of the 948 patients were physicians, fifteen being Gentiles and seven Jews. Two of these twenty-two physicians underwent amputation, each losing a leg, and one of them later underwent lumbar sympathetic ganglionectomy at the clinic. Three of the twenty-two underwent bilateral sympathetic ganglionectomy at the clinic; not one of these has been subjected

to a major amputation since. One patient who had gangrene of the toes at the time of sympathectomy has since had the toes removed. Four of these twenty-two physicians are dead, one dying of cancer; the cause of death in the other three cases was not stated.

#### COMPLICATIONS

**Thrombo-Angiitis Obliterans and Hypertension.**—Of the 948 patients who had thrombo-angiitis obliterans 147 (15.5 per cent) had hypertension. Forty-three of the 147 are dead and twenty-two of the 147 underwent amputation.

**Thrombo-Angiitis Obliterans and Diabetes.**—Ten of the patients with thrombo-angiitis obliterans also had diabetes, the diabetes being relatively mild in nine cases. Six of the ten patients were Jews. All ten patients used tobacco averaging from fifteen to forty cigarets a day.

TABLE 3.—*Thrombo-Angiitis Obliterans (1907-1937 Inclusive): Amputations at Clinic and Elsewhere*

By race	Total	Amputations					
		None		At Clinic		Elsewhere	
		No.	%	No.	%	No.	%
Jews.....	262	174	66.4	33	12.6	55	21.0
Gentiles.....	686	373	54.4	145	21.1	168	24.5
Total.....	948	547	57.7	178	18.8	223	23.5

According to race and degree of smoking

	Total			Jews			Gentiles		
	Pa- tients	No.	%	Total	No.	%	Total	No.	%
Nonsmokers	68	21	30.9	24	5	20.8	44	16	36.4
Smokers									
Grade 1...	75	35	46.7	13	8	61.5	62	27	43.5
Grade 2...	172	80	46.5	52	17	32.7	127	63	49.6
Grade 3...	161	68	42.2	50	20	40.0	111	48	43.2
Grade 4...	465	197	42.4	123	38	30.9	342	159	46.5
Total...	948	401	42.3	262	88	33.6	686	313	45.6

Major and minor amputations by race and sex

		Major		Minor	
		No.	%	No.	%
Females	Jews.....	1	100.0		
	Gentiles.....	1	14.3	6	85.7
Males	Jews.....	62	71.3	25	28.7
	Gentiles.....	212	69.3	94	30.7
Total	Jews.....	63	71.6	25	28.4
	Gentiles.....	213	68.0	100	32.0

One of the Jewish patients had a toe amputated, one of the Gentiles a leg. One of the ten died a morphine addict.

The incidence of amputation in this small group was not any greater than in the group of patients who did not have diabetes. The part diabetes mellitus plays in the presence of thrombo-angiitis obliterans is not definitely known, but the indications are that if the diabetes is not adequately controlled it may tend to aggravate the course of the thrombo-angiitis obliterans.

#### SYMPATHECTOMY IN THROMBO-ANGIITIS OBLITERANS

One hundred and ninety-three of the 948 patients underwent either cervicothoracic or lumbar sympathectomy. Twenty-eight of the patients were Jews, 165 Gentiles. Ten of the Jewish patients later underwent amputation (eight major and two minor) and forty of the Gentile patients later underwent amputation (twenty major and twenty minor). Of the total 193 patients in this group, therefore, fifty (26 per cent) were later subjected to amputation. Five of twenty-one women patients underwent bilateral lum-

bar sympathetic ganglionectomy and one of the five also underwent cervicothoracic sympathetic ganglionectomy. Eight of these twenty-one women had amputations. Four of them were nonsmokers (two major amputations, two minor amputations); the other four were smokers and all underwent minor amputation.

It is well recognized that sympathectomy does not cure thrombo-angiitis obliterans. Probably it does not

TABLE 4.—*Thrombo-Angiitis Obliterans (1907-1937 Inclusive)*

Age, Years	Amputations at Various Periods After Onset of the Condition								
	Three Years			Five Years			Ten Years		
	Amputations			Amputations			Amputations		
	Total Patients	Number Traced	Per Cent of Those Traced	Total Patients	Number Traced	Per Cent of Those Traced	Total Patients	Number Traced	Per Cent of Those Traced
10-19.....	2	2	0	2	2	0	0	0	0
20-29.....	78	69	25	75	63	52.4	49	36	77.8
30-39.....	272	230	68	261	210	82	158	121	75
40-49.....	321	265	82	304	243	96	148	118	74
50-59.....	140	117	38	129	100	35	71	55	21
60-69.....	13	9	2	12	9	22.2	5	4	2
70-79.....	2	2	0	2	1	0	2	0	0
Total.....	828	694	215	785	623	248	433	334	200

even alter the course of the disease in the blood vessels. It does, however, bring about the maximal blood flow to the sympathectomized extremities and for that reason is still the most logical surgical procedure in properly selected cases for increasing the blood supply.

#### CAUSES OF DEATH

One hundred and seventy-five of the 948 patients with thrombo-angiitis obliterans are known to be dead. Five of these were women. It is interesting to note that coronary heart disease ranked first as the cause of death, forty-seven (27 per cent) of the 175 patients having died of it. An additional twelve patients died of cerebral hemorrhage. Twelve patients died with gangrene or following amputation for gangrene, and seven died of fatal pulmonary embolism. The others died of known but unrelated causes.

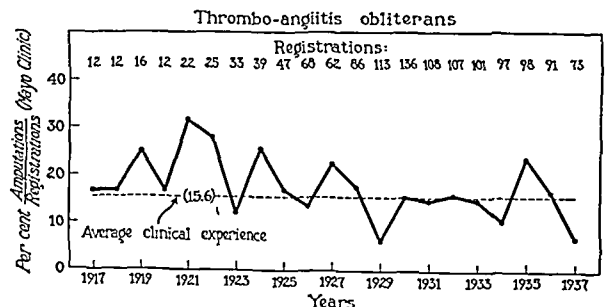


Fig. 3.—Incidence of amputations for thrombo-angiitis obliterans according to registrations.

#### PROGNOSIS

While in this study I have been able to tabulate many facts regarding this series of cases of thrombo-angiitis, no one could ever tabulate the loss of time and money, the pain and suffering and the tragedy of the loss of limbs incurred by these unfortunate persons. When one contemplates the large number of those who underwent major amputation, frequently of both legs and

occasionally of both arms, and who yet were able to carry on with a smile, one cannot help but think of Tennyson's lines "That men may rise on stepping-stones of their dead selves to higher things."

What, then, are the important factors which determine whether a person with thrombo-angiitis obliterans will live out his life expectancy walking on two feet, or whether he will fall into the unfortunate group whose extremities will have to be amputated? I believe that early diagnosis and thorough education of the patient concerning the nature of his disease and the care of his extremities will accomplish more in this respect than all other factors at the physician's command. Early diagnosis is important in order that the individual can avoid unnecessary delay in carrying out prophylactic measures to prevent the occurrence of gangrene. When it is recalled that at least 20 per cent of the patients who have come to the clinic with gangrene have had incisions made or nails removed for supposed infections of the digits, it becomes apparent that a working knowledge of the early signs and symptoms of thrombo-angiitis obliterans still is not widespread among members of the medical profession. The most frequent errors in diagnosis consist in mistaking claudication in the foot for evidence of arthritis or fallen arches and the abnormal rubor of the toes for evidence of infection. Pain in the arch of the foot on exercise suggests a structural defect in the bony support; hence most patients with thrombo-angiitis obliterans have had three or four pairs of arch supporters. Fortunately this error is much less evident now than it was ten years ago.

The essential point to establish, in the presence of symptoms referable to the hands, feet or legs, is whether the complaint is attributable to disease of the vessels and, if it is, whether the process is occlusive or vasomotor. The distinction between occlusive arterial disease and vasomotor disturbances can be made with accuracy in 95 per cent of cases by determining by simple palpation the presence or absence of pulsations in the four palpable arteries of the leg or in the two palpable arteries of the wrist. If the arteries are occluded there is more than a 90 per cent chance that the condition is thrombo-angiitis obliterans or arteriosclerosis obliterans. In the fifth decade of life the necessity for distinguishing between these two conditions is, of course, more or less academic, since the problem of treatment is, with a few well defined exceptions, the same. The chief difficulty in diagnosing localized vascular disease of the extremities is in distinguishing the vasomotor or functional type from the organic type, particularly when the lesions are associated.

#### EDUCATION OF THE PATIENT

It is just as important to educate the patient who has thrombo-angiitis obliterans regarding the nature of his disease as it is to instruct the patient who has diabetes mellitus regarding his diet. This cannot be accomplished in a few hours or even in a few days. Patients must be cautioned to avoid trauma and undue exposure to cold. Patients should also be taught to avoid crushing or bruising the feet or toes, and they should be instructed in the proper care of scratches, cuts, cracks, blisters and burns. The slightest abrasion should be carefully treated and regarded as if it were a major injury. New shoes should be worn for only a half hour to an hour the first day, and considerable time should be spent in breaking in such shoes. Soft woolen stock-

ings should always be worn in cold weather. On many occasions simple abrasions produced by the wearing of new shoes have resulted in the formation of ulcers and in gangrene and amputation. Care of the toe nails is extremely important; it becomes more and more important as the blood supply to the digits decreases. Toe nails should be cut straight across, after being soaked in warm water, and they should be scrupulously but carefully cleaned. Corns, calluses and bunions should not be cut. Removal of ingrown toenails and minor operations on the toes in many cases have produced gangrene which in time has been followed by amputation. Such minor surgical procedures should be avoided except in rare instances and should then be performed only by a surgeon who is familiar with the problems involved in occlusive arterial disease.

Because of the poor blood supply to the feet, patients who have occlusive arterial disease may sustain injuries more readily than normal persons. They are also more susceptible to ill effects from exposure to cold. From the standpoint of cleanliness, the feet should be washed carefully and dried gently with a soft towel. Extreme care should be used in drying the skin between the toes. Brisk rubbing with a rough towel in many instances has produced ulcers. The occasional application to the feet and toes of a 50 per cent solution of alcohol is desirable, but this should not be used to excess. If the feet are excessively dry, or if the skin tends to crack or undergo scaling, hydrous wool fat or theobroma oil can be rubbed in gently to soften the skin. In numerous cases gangrene has been caused by the use of strong disinfectants, chemical compounds, ointments, corn cures and remedies for athlete's foot. It is unwise to use iodine, saponated solution of cresol, carbolated petrolatum or similar preparations as local disinfectants. Athlete's foot, which is a form of ringworm or trichophytosis, is frequently present in cases of thrombo-angiitis obliterans or arteriosclerosis obliterans and is usually worse in warm weather. This condition should receive appropriate care when it develops, as it is frequently the starting point of ulceration and gangrene between the toes. A safe method for treating athlete's foot is to soak the feet for a half hour each day in a 1:8,000 solution of potassium permanganate. This solution should be made up fresh for each soaking.

In spite of all the care which a patient may take, however, injuries to the toes and feet occasionally occur. When such a lesion develops, absolute rest in bed is indicated. In many a case in which gangrene has developed and the patient has lost an extremity he could perhaps have avoided such a calamity if he had taken the proper precautions early.

*Smoking.*—Mark Twain is reputed to have remarked that to stop smoking was the easiest thing he ever did, and he said he ought to know for he had done it a thousand times. Most patients who have thrombo-angiitis obliterans have had the same good intentions but have continued to smoke. Of the 948 patients, so far as I can determine only 106 stopped smoking. Eleven of these 106 expressed the opinion that the use of tobacco had been harmful to them. This phase of the problem is still being investigated.

About 50 per cent of those who stopped for varying periods resumed the habit, feeling that their symptoms were not improved after they had stopped. A rather large number, on the other hand, were convinced that smoking was the cause of their disease and said that they were greatly benefited after they stopped smoking.

Most of these gained weight, often from 15 to 20 pounds (7 to 9 Kg.) or more after they stopped smoking.

We at the clinic are of the firm conviction that all patients who have thrombo-angiitis obliterans should stop smoking. This, of course, brings up an interesting point as to the effects of tobacco on prognosis. A number of investigations have held that tobacco is the primary etiologic agent in the production of this disease, and yet, in this series, sixty-eight of the 948 patients had never used tobacco. Obviously the use of tobacco cannot be the cause of the disease, but it is evident, in the majority of cases, that excessive smoking does make the symptoms worse, although there are numerous exceptions even to this rule.

#### SUMMARY AND CONCLUSIONS

A total of 948 patients who had thrombo-angiitis obliterans were observed at the clinic from 1907 to 1937 inclusive. These patients came from every state in the Union except three and from ten foreign countries. More than twenty-eight different nationalities were represented. Two hundred and sixty-two (28 per cent) of the patients were Jews; 686 were Gentiles. The same fundamental pathologic process was present in all cases, and the signs and symptoms, as well as the clinical course of the disease, were strikingly similar. Twenty-one of the patients were women, the remaining 927 men; in other words, approximately 98 per cent of the patients were men. The mean age of the men was 41.8 years, of the women 38.8 years.

Of the 948 patients in the series 880 (93 per cent) were cigarette smokers. Of the 262 Jewish patients eighty-eight (33.6 per cent) underwent amputation, and of the 686 Gentile patients 313 (45.6 per cent) underwent amputation. Thus, 401 of the 948 patients underwent amputation either at the clinic or elsewhere. Eighty-five patients underwent bilateral amputation of the legs; sixteen of these patients were Jews and the remaining sixty-nine were Gentiles.

A study of amputations for three, five and ten year periods after the onset of the disease (table 4) indicates that approximately 70 per cent of patients will go for a period of three years from the onset without the necessity of amputation, whereas only 60 per cent will go for a period of five years and only 40 per cent for a period of ten years without being obliged to undergo amputation.

Perhaps the most important factors which determine whether a person who has thrombo-angiitis obliterans will continue to walk on two feet throughout life are early diagnosis and thorough education of the patient concerning the nature of his disease and the care of his extremities.

#### ABSTRACT OF DISCUSSION

DR. F. E. BOLLAERT, East Moline, Ill.: May I inquire about the recent treatment by suction pressure as well as the hyperemia treatment of these cases?

DR. BAYARD T. HORTON, Rochester, Minn.: The alternate suction and pressure apparatus is being used rather widely and we have used it for a number of years. I do not believe that we get any better results from the use of this machine than we can get from other simpler methods. I prefer the use of the Saunders bed to this alternate suction and pressure apparatus. With the use of the Saunders bed the patient must be kept in an environmental temperature of 82 degrees or above because one cannot get rid of vasospasm, particularly in the feet, unless the environmental temperature is at or above that level.

## THE SURGICAL PATHOLOGY OF NASAL SINUSITIS

HERMAN SEMENOV, M.D.

LOS ANGELES

The first essential in the treatment of nasal sinusitis is an exact differential diagnosis of the surgical and nonsurgical types of disease condition present in the lining membranes. A lack of precise histopathologic knowledge in the past has led to the indiscriminate removal of tissues essential to the physiology of the nose and accessory sinuses. As every one knows, this has been attended by a striking array of contradictory results.

The purpose of this report is to recount in as much detail as possible the known types of sinusitis, the effects of allergy on the course of the sinus disease, the separation of reversible inflammatory from irreversible degenerative changes, and the character of the lining that forms after radical operations. The chief desideratum is a working principle which will delineate the types of disease present in every case and indicate the most appropriate treatment for each. The method of choice, selected from the several methods of treatment at hand, should completely remove the underlying disorder and most nearly conserve the normal functions of the nose and accessory sinuses.

#### MATERIAL AND METHODS

In this undertaking the histology and physiology of the sinuses were carefully reviewed and numerous normal membranes were taken from cadavers for measurement with the micrometer. The surgical specimens were measured at the principal point of disease and the results arbitrarily correlated with the exudative, proliferative and degenerative changes noted microscopically.

The material for the present report embraces more than a thousand sections collected and examined during the past ten years. The membranes were removed in one piece by careful subperiosteal dissection (Caldwell-Luc, transantral and external frontal ethmoidal operations), mounted on cardboard supports or stretched over wads of cotton and fixed in 10 per cent solution of formaldehyde (fig. 1). They were sectioned by the paraffin method, stained as a routine with hematoxylin and eosin, occasionally with other methods of special staining, and in numerous instances with the Gram bacterial stain. The bacteriology of 400 sinuses was investigated by making swabs at the time of operation. Tissue cultures were made from 120 sinuses by grinding the membranes in sterile sand.

#### INCIDENCE OF ALLERGY IN SURGICAL CASES

1. *Nonallergic Cases* (47.6 per cent).—These include cases with a negative history of hay fever or asthma, absence of characteristic rhinologic signs (vasomotor rhinitis, bluish appearance of the turbinates) and lack of eosinophilia in the histologic preparations.

Owing to lack of space, this article has been abbreviated for publication in *THE JOURNAL*. The complete article appears in the author's reprints.

Read before the Section on Laryngology, Otology and Rhinology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 17, 1938.

This work was started in 1928 under the facilities of the Nebble Wiley Jones Fellowship in Pathology in the Department of Pathology of the University of Oregon Medical School in collaboration with Dr. Frank B. Ristner.

2. *Manifest Allergic Cases* (17 per cent).—These include cases with history, symptoms or signs of hay fever or asthma, suggestive bluish appearance of the turbinates, polypoid degeneration of the nasal mucosa and microscopic appearance of tissue eosinophilia, edema of the submucosa, hyaline degeneration of the basement membrane and mucoid degeneration of the overlying epithelium.

3. *Equivocal Allergic Cases* (35.4 per cent).—This group includes a large number of latent allergic conditions and a more or less variable number of pseudo-allergic specimens in which the history was uncertain, vague or incomplete but in which microscopic examination showed tissue eosinophilia in association with one or more other histopathologic signs sufficient to warrant a presumptive diagnosis of latent allergy, if one were so inclined.

Nearly 52.4 per cent of the surgical cases presented histopathologic signs which suggested the possibility

dence of cysts and abscesses (50 per cent) was even greater in the cases in which polypoid degeneration developed (thickening 3 to 10 mm. or more). Bacteria were demonstrated by culture of the fluid in nearly half of the serous cysts. Typical cases with reports of the bacteriology and pathologic histology of nonpurulent sinusitis and several interesting cases of latent sinus infection without clinical signs of suppuration have been described in previous publications.<sup>2</sup>

#### BACTERIOPATHOLOGY

Mixed infections of two or more organisms occurred in 80 per cent of the cases of chronic sinusitis. Streptococci predominated in both the swabs and the tissue cultures. They were present in 94.5 per cent of the cases. Staphylococci appeared in 70 per cent. Sixty-eight per cent of the chronic sinuses contained alpha and beta hemolytic streptococci, 14 per cent the non-hemolytic *Streptococcus viridans* (alpha), and 18 per cent the nonhemolytic streptococcus (gamma). In addition to and frequently in combination with the streptococci the chronic sinuses contained staphylococci, *Micrococcus catarrhalis*, pneumococci, Friedländer's

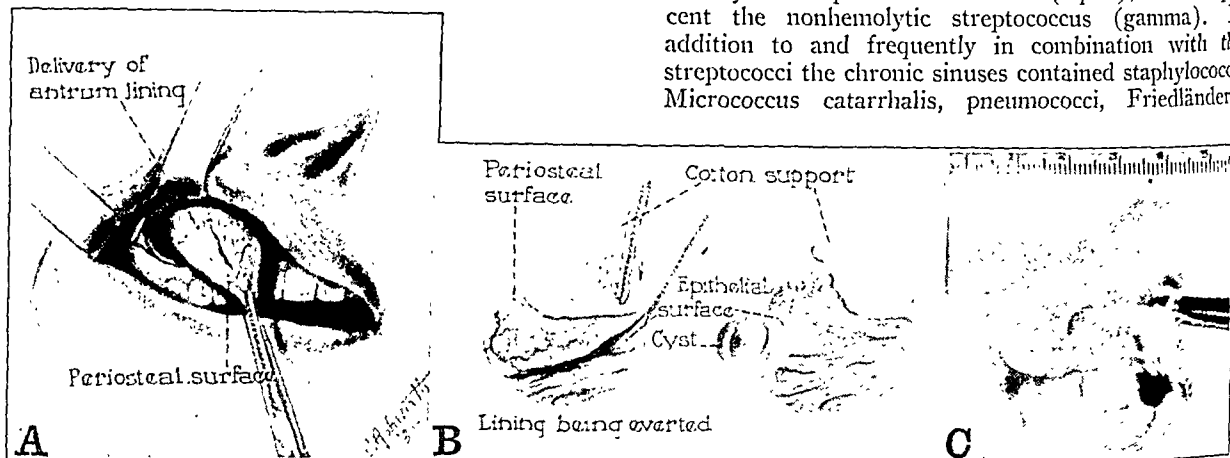


Fig. 1.—A, removal of specimen of sinus; B, method of mounting on cotton; C, specimen showing large serous mesothelial cyst.

of an underlying allergy. Of this number at least 17 per cent were definitely allergic. More than 70 per cent of the obviously allergic cases presented superimposed suppurating infection.

Purulent sinusitis with exudate in the nose, diagnostic puncture (cytologic examination) and histologic

bacilli, influenza bacilli, colon bacilli, diphtheroids and Streptothrix.

The virulence of the streptococci was tested in twenty rabbits and found to be pathogenic in seventeen. Various lesions were produced in the brain, heart, liver, kidneys, arteries and articular joints. Experimental arteritis and arteriosclerosis were produced in five rabbits with the hemolytic *Streptococcus anginosus* from a case of chronic sphenoiditis and large inguinal abscesses and myocardial and hepatic changes in two monkeys that were inoculated with the nonhemolytic *Streptococcus mitis* from a chronically infected antrum.<sup>3</sup>

A pure culture containing only one type of organism was found in only 20 per cent of the sinuses. Beta hemolytic streptococci appeared most frequently in purulent sinusitis. Staphylococci, especially the hemolytic type, also produced marked suppuration.

#### NORMAL HISTOLOGY OF THE MUCOPERIOSTEUM OF THE SINUSES

The sinus lining is less robust, less vascular and less glandular than the schneiderian membrane (fig. 2). Erectile tissue is lacking, the stroma is quite weak and rudimentary, and the entire lining is much thinner than the nasal mucous membrane.

sections was present in 72 per cent of all the cases. Nonpurulent sinusitis (hyperplastic, polypoid and cystic) was present in the remaining 28 per cent.

Nonpurulent hyperplastic, polypoid and cystic degeneration of the sinuses may arise as a consequence of either a suppurative process which has subsided or a nonsuppurative allergic process. Abscesses formed in 10 per cent and cysts in 33 per cent of the hyperplastic sinus membranes (thickening 1 to 2 mm.). The inci-

TABLE 1.—Chronic Sinusitis in Relation to Allergy

	Distribution of 500 Cases					
	Purulent Sinusitis		Nonpurulent Sinusitis		Incidence of Allergy	
	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
Constitutional Background						
.. .. .	185	37	53	10.6	283*	47.6
.. .. .	60	12	25	5.0	85	17.0
.. .. .	115	23	62	12.4	177	35.4
Surgical pathology.....	360	72	140	28.0	500	100.0

\* Nonallergic.

2. Kistner, F. B.: Chronic Nonpurulent Sinusitis and Its Clinical Significance, *Ann. Otol., Rhin. & Laryng.* 38: 795 (Sept.) 1929; *Histopathology and Bacteriology of Sinusitis*, *Arch. Otolaryng.* 13: 225 (Feb.) 1931. Kistner and Semenov.  
3. Benson, R. L.; Smith, K. G., and Semenov, Herman: Experimental Arteritis and Arteriosclerosis Associated with Streptococcal Inoculations, *Arch. Path.* 12: 924, (Dec.) 1931.

The mucoperiosteum is composed of a single layer of pseudostratified ciliated columnar epithelium, which rests on a delicate basement membrane, and two layers of connective tissue: (1) a loose subepithelial areolar layer and (2) a compact periosteal layer (fig. 3 *B*). Under normal conditions there are very few goblet cells in the epithelium and no signs of edema or round cell infiltration in the submucosa.

TABLE 2.—Pure Cultures

Bacteriology	Pathology	
	Purulent	Nonpurulent
Hemolytic streptococcus beta.....	18	1
Hemolytic streptococcus alpha.....	7	6
Nonhemolytic streptococcus viridans alpha...	12	6
Nonhemolytic streptococcus gamma.....	14	3
Staphylococcus .....	11	3
	62 (76%)	19 (24%)
Total.....	81	

The normal sinus membrane is very thin, about 0.1 mm. in thickness, and may be compared to the membrana tympani, which is also 0.1 mm. in thickness.

The loose subepithelial layer has wide tissue spaces and usually becomes extremely edematous. The edema frequently ruptures the fibrils of areolar connective tissue and leads to the formation of mesothelial cysts. There is an astonishing degree of variation in the histologic structure of the subepithelial stroma. Some membranes are composed entirely of areolar tissue and these are prone to develop marked degenerative changes after trivial sinusitis; others are composed of a tougher periosteal type of stroma and successfully resist infection for many years (fig. 3).

The glands in the mucous membrane of the sinuses are relatively scarce. In the ethmoidal, sphenoidal and frontal sinuses submucous glands appear only in the neighborhood of the ostia.

In general the membrane of the maxillary sinus differs from that of the ethmoidal, the sphenoidal and the

ing of the antrum is loosely attached to the superior, posterior and lateral walls by delicate strands of connective tissue. The frontal membrane (pneumatization quite late in life) appears to be the most rudimentary of all the paranasal sinuses.

There are very few blood vessels in the mucosa of the sinuses and the circulation seems relatively poor.

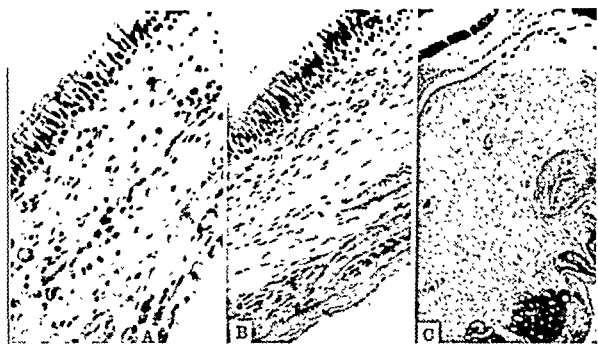


Fig. 3.—A, mucosa composed entirely of loose areolar tissue with rudimentary periosteum; B, normal mucoperiosteal arrangement; C, dense fibrous submucosa with very little loose tissue.

This may in part account for a slower rate of healing and a higher incidence of degenerative changes.

#### HISTOPATHOLOGY OF SINUSITIS

Increase in thickness of the membrane is caused partly by the cellular infiltration, partly by the edema of the connective tissue and partly by the proliferation of fibroblasts, which generally give the stroma a myxomatous appearance.

**Cellular Exudation.**—The leukocytic sequence in acute inflammation consists of an initial polymorphonuclear infiltration which is followed immediately by lymphocytes, eosinophils and mononuclear macrophages. All types of cells may be present in the subepithelial tissues within a period of fifty hours after the onset of the inflammatory reaction. The polymorphonuclear cells pass through the epithelium in great numbers and predominate in the pus that forms on the surface of the membranes. The lymphocytes and

TABLE 3.—Thickness of Mucous Membranes of Sinuses

	Normal Variations in Millimeters	Pathologic Thickening in Millimeters
Maxillary sinus		
Medial wall.....	0.3 - 1.0	1.0 -20.0
Lateral wall.....	0.1 - 0.5	1.0 -20.0
Frontal sinus.....	0.07- 0.3	1.0 - 4.0
Ethmoidal sinus.....	0.05- 0.4	1.0 - 5.0
Sphenoidal sinus.....	0.07- 0.5	1.0 - 5.0

plasma cells are inclined to remain within the tissues and for this reason predominate in the submucosal picture.

In 1927 Finck<sup>5</sup> noted the presence of eosinophilic infiltration in the nasal mucosa of allergic patients. In 1929 Kistner and I<sup>6</sup> confirmed this finding in the sinuses and with a few exceptions during the past ten years have found eosinophilic infiltration constantly present in allergic membranes. Numerous investiga-



Fig. 2.—Normal lining of ethmoidal sinus (E) compared with normal mucosa of middle turbinate attachment (T) and septum (S).

frontal only on its medial walls, where the structure is more complex owing to a rich supply of blood vessels and glands, which may be attributed to the earlier embryonic history of this part (paleosinus) in the development of pneumatization. The mucosa of the lateral wall of the antrum (neosinus) is poorly developed and resembles the frontal sinus in many respects. The lin-

5. Finck, H. P.: Tissue Changes in the Nasal Mucosa, *Laryngoscope* 37: 783-797 (Nov.) 1927.

6. Kistner, F. B., and Semenov, Herman: Pathology of Sinusitis, *Tr. Pacific Coast Oto-Ophthalm. Soc.*, 1929; *Ann. Otol., Rhin. & Laryng.* 38: 978 (Dec.) 1929.



tors, notably Hansel,<sup>7</sup> have studied the presence of eosinophils in smears of the nasal discharge and it is now a well established routine diagnostic method.

**Mucoid Exudate.**—The mucous membranes of the sinuses, as their name indicates, are moistened by a mucus-containing secretion. Under normal conditions only a small quantity of a limpid mucus is formed, but with the advent of irritation a more viscid secretion



Fig. 4.—A, goblet cells and mucoid degeneration in catarrhal sinusitis; B, hyperplastic ciliated epithelium in purulent sinusitis; C, epithelial metaplasia with leukocytic emigration.

appears. Most of the viscid mucus found in the sinuses is actually formed by mucoid degeneration of the surface epithelium.

Mucoid degeneration (fig. 4 A) is a very common process in the epithelium of the sinuses. It is manifest by the appearance of an abnormal number of goblet cells. The cilia are lost under these conditions and wide areas of sloughing epithelium, presenting only a remnant of basal cells, are frequently seen in allergic sinuses. This is one of the reasons why allergic sinuses are so frequently infected. In purulent sinusitis some areas show ciliated columnar cells, others hyperplasia (fig. 4 B), metaplasia (fig. 4 C) and focal necrosis (fig. 5). Hypertrophy and hyperplasia appear as defense reactions after chronic mucoid degeneration runs a protracted course.

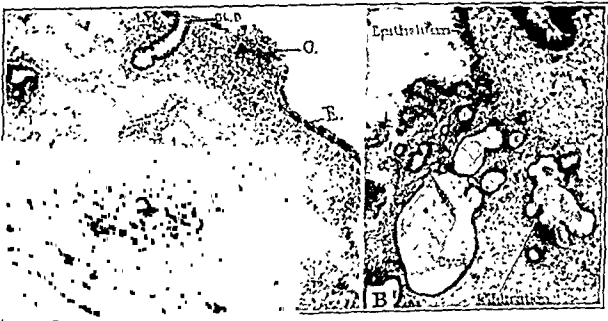


Fig. 5.—Chronic purulent sinusitis with infection of the glands, edema, infiltration and necrosis of epithelium and cystic dilatation.

**Proliferative Changes.**—Hyperplasia is present when there is an increase in the number of cellular elements. Hyperplastic processes in all cases produce a tissue similar to that of the original part; hyperplasia of the epithelium gives rise to new epithelial cells, that of the glands to new gland cells, that of the connective tissue to new connective tissue cells, and so on. Hyperplasia of the stroma clearly follows acute inflammatory processes and bears the same relation to injury that

the cicatrix and healing wound do to the granulation tissue from which they spring.

Proliferation of the connective tissue produces the greater part of the irreversible thickening of the sinus membranes (fig. 6). There is an increase in the number of fibroblasts and spindle and stellate cells. The subepithelial areolar layer tends to undergo polypoid degeneration (edema and a soft myxomatous tissue), but the more compact periosteal layer is more resistant to edema and infiltration. The periosteal portion tends to thicken and become more or less tough and fibrous during the course of chronic sinusitis.

The pathologic changes in hyperplastic sinusitis may be circumscribed or diffuse, involving either certain parts or the entire lining of the sinuses (figs. 6 to 9). The mild form of hyperplastic sinusitis tends to run a slow, insidious course with remissions and exacerbations. The exudative and edematous changes are

TABLE 4.—Incidence of Degenerative Changes in Relation to Exudation and Thickening: 422 Cases

Type of Cellular Exudation	Purulent Sinusitis				Nonpurulent Sinusitis			
	Round Cells, Neutrophils		Round Cells, Neutrophils, Eosinophils		Lymphocytes, Plasma Cells		Lymphocytes, Plasma Cells, Eosinophils	
	Per Cases	Cent	Per Cases	Cent	Per Cases	Cent	Per Cases	Cent
Thickening, 1-2 mm.								
Cysts.....	3	5.3	1	1.9	6	20.0	13	27.5
Abscesses.....	3	5.3	1	1.9	3	10.0	4	8.5
Degeneration (irreversible).....	6	10.6	2	3.8	9	30.0	17	36.0
Hyperplasia (edematous).....	50	89.4	50	96.2	21	70.0	30	64.0
Totals.....	50		52		30		47	
Thickening, 2-5 mm.								
Cysts.....	16	19.0	38	35.0	11	50.0	15	47.0
Abscesses.....	6	7.0	13	13.0	0		0	
Degeneration (irreversible).....	22	26.0	51	51.0	11	50.0	15	47.0
Hyperplasia (polypoid edematous).....	61	74.0	49	49.0	11	50.0	17	52.0
Totals.....	63		100		22		32	

reversible and may subside completely after the exciting causes (allergy or infection) are removed, or they may continue on for weeks, months or even years without giving rise to symptoms. In the latent form of hyperplastic sinusitis, washings from the antrum usually contain numerous degenerating epithelial cells on cytologic examination.

DEGENERATIVE CHANGES

1. **Retention Cysts.**—Obstruction of the gland ducts by leukocytic infiltration (fig. 5) initiates the formation of retention cysts, and as each acinus becomes cystic it encroaches on the adjacent glands; eventually the dilated tubules rupture into one another. The interior of a retention cyst is lined with epithelium in various stages of degeneration. Sometimes there are areas devoid of epithelium bordering on areas of flattened cells which gradually pass over into columnar cells, and finally one may find mucous or goblet cells. It is probable that the epithelial variations represent stages in the cystic evolution. Retention cysts contain a thick mucoid material which sometimes is mixed with concentric deposits of epithelial debris and leukocytes.

7. Hansel, F. K.: Allergy of the Nose and Paranasal Sinuses, St. Louis, C. V. Mosby Company, 1936.

2. *Mesothelial Cysts*.—When the tissue spaces of the loose areolar stroma become extremely edematous, they frequently rupture and form large cystic cavities. These cysts have no epithelial lining. They are usually thin walled and in the absence of suppuration are filled with a clear amber fluid (fig. 1 C).

Cystic degeneration appeared in one third of all the cases of chronic sinusitis. It was greater in the mucous membranes that were more than 2 mm. in thickness (50 per cent), especially in the allergic specimens. Normal glands were found in only 15 per cent and cystic dilatation with abscess formation in 85 per cent of the manifest allergic cases. Abscesses appeared in from 5 to 15 per cent of the purulent sinuses.

3. *Polypoid Degeneration*.—Polypoid degeneration, whether it is bacterial, allergic, catarrhal or suppurative, is always characterized by great edema, which may be attributed to impaired circulation, abnormal capillary permeability and lymphatic obstruction in a delicate stroma. There are many other factors responsible for this condition, but the loose histologic structure of the mucosa of the sinuses and the presence of chronic edema (allergy or chronic infection) are the evident predisposing factors.

Polyps consist of a water-logged myxomatous connective tissue in both the nose and the paranasal sinuses. Eosinophilia was found in more than two thirds of the

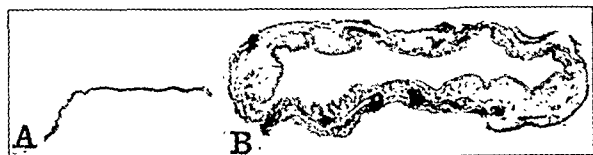


Fig. 6.—A, normal thickness of lining; B, hyperplastic sphenoidal membrane, ten times normal thickness. Figures 6, 7, 8 and 9 are reduced from photomicrographs with a magnification of ten diameters.

polypoid specimens. These cases were considered allergic; no evidence of eosinophilia was found in one third of the cases and the pathologic condition was considered nonallergic.

In a recent publication Kern and Schenck<sup>8</sup> stated that allergy is a constant factor in the etiology of nasal polypi. They believe that nearly 100 per cent of mucous polyps are allergic in origin. Walsh and Lindsay<sup>9</sup> in a well controlled investigation of seventy-five cases of nasal polyposis found that some were associated with allergy and others with nonallergic infection of the nasal accessory sinuses. The nonallergic polypi are usually unilateral, and removal is followed by better results than removal of allergic polypi, which are frequently bilateral.

Polypoid degeneration throws the surface of the mucous membrane into crypts and pockets, which retain much infection and interfere with ciliary action. Non-allergic polypoid sinusitis demonstrating mesothelial cystic degeneration may be seen in figure 7. Allergic sinusitis with extensive formation of mucus and marked polypoid edema of the loose areolar tissue may be seen in figure 8. Marked polypoid degeneration with a large mucous cyst and a large mesothelial cyst may be seen in figure 9. This specimen is from a patient with

allergy and demonstrates the great tendency of allergic sinusitis to develop into pronounced degenerative changes.

Choanal polyps sometimes form in the sinuses, especially in the antrum, and extrude through the ostium into the nasopharynx. The origin of these polyps is frequently on the lateral wall of the antrum (fig. 10). I have often wondered why this should be so; one would ordinarily expect polypi to begin near the ostium



Fig. 7.—Polypoid degeneration in chronic purulent sinusitis, nonallergic. Thickening from ten to forty times normal.

where the greatest amount of irritation and discharge is to be seen. The answer lies, I believe, in the histology and embryology of the antrum. The lateral portion, as has already been stated, is extremely thin, changes quite late in life and belongs to the rudimentary neosinus. It is therefore quite delicate and subject to greater degenerative changes, since the blood supply and lymphatic drainage of this region are so vulnerable.

According to André,<sup>10</sup> Grunwald<sup>11</sup> and Mullin and Ryder,<sup>12</sup> the lymphatic channels lie in the membranes and follow a circuitous course to the ostium. Obstructive processes, either vasomotor, allergic, infiltrative or inflammatory, have many opportunities to interfere with this extended line of communication and may easily give rise to back pressure, chronic hydrops mucosae and polypoid swelling on the lateral wall of the antrum.

Considerable absorption of bone and osteoporosis accompany polypoid degeneration. Every one is famil-



Fig. 8.—Polypoid allergic sinusitis from fifteen to fifty times normal thickness.

iar with osteoporosis of the middle turbinate in polypoid degeneration of this structure. I have several times seen extreme absorption in the canine fossa as a result of the chronic hyperemia and stasis associated with polypoid degeneration within the antrum. A pyogenic

8. Kern, R. A., and Schenck, H. P.: Allergy a Constant Factor in the Etiology of the So-Called Mucous Nasal Polyp, *J. Allergy* 4:485 (Sept.) 1933.

9. Walsh, T. E., and Lindsay, J. R.: Cytology of Nasal Polypi, *Arch. Otolaryng.* 20:649 (Nov.) 1934.

10. André, J. M.: Contribution à l'étude des lymphatiques du nez et des fosses nasales, Thesis, Paris, 1905; *Recherches sur les lymphatiques du nez et des fosses nasales*, *Ann. de mal. de l'oreille, du larynx*, etc. 31:425, 1908.

11. Grunwald, L.: Die Lymphgefäße der Nebenhöhlen der Nase, *Arch. f. Laryng. u. Rhin.* 23:1, 1910.

12. Mullin, W. V., and Ryder, C. T.: Studies on the Lymph Drainage of the Accessory Nasal Sinuses, *Laryngoscope* 31:158 (March) 1921.

process seldom creates this condition. As a matter of fact, pyogenic inflammation often leads to formation of new bone and fibrosis.

#### REGENERATION AND HEALING OF THE MUCOUS MEMBRANE OF THE SINUSES

There are few, if any, references in the available literature to the microscopic appearance of the mucous membranes of the sinuses after inflammation has subsided and complete healing has resulted. The question frequently arises Does sinusitis ever heal completely and what happens when it heals without operation? These questions may be answered by the following case:

A man aged 50 had apparently recovered without surgical treatment from a chronic mucopurulent sinusitis of twenty-five years' duration. For a period of four years he was free from colds, nasal discharge and sinusal symptoms. X-ray examination of the sinuses revealed definite thickening and blurring of the antrums, ethmoids and sphenoids. The mucous membranes were removed, sectioned and found to be many times the normal thickness. When examined under the microscope, the epithelium was perfectly normal. The submucous connective tissue, instead of being loose and areolar, was thick and fibrous (fig. 3C).

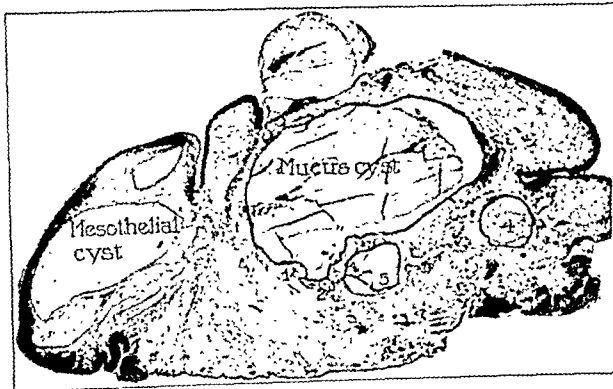


Fig. 9.—Polypoid and cystic degeneration in allergic sinusitis, showing mesothelial cyst and retention cyst. From fifty to seventy times the normal thickness.

The stroma was fully 2 mm. thick. There were no signs of edema, inflammation or degeneration. The glands were compact and surrounded by firm connective tissue.

This interesting mucoperiosteum apparently became tougher and stronger as the years went on. Similar changes have been noted in the ethmoidal, sphenoidal and maxillary membranes in several other cases. Healing by fibrosis is a desirable end result as far as the sinuses are concerned.

*Postoperative Repair and Regeneration of Sinus Lining.*—The blood clot on the denuded osseous wall gradually organizes and becomes converted into scar tissue. Epithelium spreads from the bordering nasal mucosa and gradually covers the surface of the scar tissue.

In previous publications Kistner and I<sup>13</sup> called attention to the presence of scar tissue and the variability of the epithelial regeneration, especially the cilia. This does not mean that the cilia are absent altogether, for we have always maintained that healing varies from place to place and from person to person and there is no reason why it should not produce perfectly normal epithelium in some cases. From a practical point of view, however, the postoperative membrane is a poor

substitute for the original mucous membrane of the normal sinus. Hilding's<sup>14</sup> physiologic experiments in the frontal sinuses of dogs demonstrate the existence of impaired ciliary function in those areas in which the mucous membrane has been removed and permitted to regenerate. This postoperative condition of the lining, on the other hand, is much better than a pathologic sinus full of polypi, cysts and abscesses, but one should not justify radical surgery on the assumption that the postoperative condition of the tissue is normal sinus mucoperiosteum.

#### COMMENT

Anatomic obstructions, such as deflections of the nasal septum, concha bullosa and similar abnormalities, are predisposing factors in the etiology of chronic sinusitis. Repeated attacks of nasal congestion with thickening and polypoid degeneration are frequently due to an allergic constitution. Allergy is a predisposing factor in nearly half of the cases of sinusitis. Trauma, epidemic colds and bacterial invasion by extension from neighboring foci of infection such as dental abscesses, oro-antral fistulas and osteomyelitis of the jaw have long been known to be exciting factors.

The treatment of chronic sinusitis may terminate successfully after the offending obstructions and hypersensitiveness to extrinsic allergens have been corrected.

Exudative changes are frequently reversible when ventilation and drainage are established. Degenerative changes with pronounced thickening of the mucous membrane rarely respond to simple drainage and usually require radical surgery of the sinuses (fig. 10B). A subacute mucopurulent sinusitis often responds to the Proetz displacement method of irrigation and suction. A suppurative infection, however, with empyema of the sinuses may require surgical intervention before adequate drainage is obtained. Chronic purulent sinusitis that fails to respond to conservative methods of drainage invariably shows deep seated infection of the glands and cystic degeneration of the submucosa (fig. 5).

Nonpurulent hyperplastic sinusitis rarely requires surgical intervention. Nearly two thirds of the cases are due to allergy, especially when a bilateral process is present. The allergic constitution predisposes one to pansinusitis and degenerative changes of the mucous membrane of the entire upper respiratory tract. For this reason it is well to treat the underlying allergic condition before serious consideration is given to surgical intervention. Purulent sinusitis in an allergic individual should be treated simply as a local problem of drainage. The results, however, are not as brilliant as in nonallergic persons. Healing is more sluggish and polypoid edema tends to appear even in the granulation tissue. With this in mind I believe that the statistics of the future will show a higher incidence of cured sinusitis once the allergic conditions are recognized as such and treated with the same consideration that is afforded syphilitic and tuberculous conditions.

#### SUMMARY

1. The microscopic changes of the sinusal mucoperiosteum in several hundred surgical specimens show that thickening in excess of 2 mm. is associated with deep seated degenerative changes in 50 per cent of the cases.

13. Semenov, Herman, and Kistner, F. B.: Repair in the Paranasal Sinuses of Man Following Removal of Mucous Membrane Lining, *Proc. Soc. Exper. Biol. & Med.* 27: 322 (Jan.) 1930. Kistner, footnote 2, second reference.

14. Hilding, Anderson: Experimental Surgery of the Nose and Sinuses: II. Gross Results Following the Removal of the Intersinus Septum and of Strips of Mucous Membrane from the Frontal Sinus of the Dog. *Arch. Otolaryng.* 17: 321 (March) 1933.

2. Purulent sinusitis constitutes 72 per cent of the cases. Nonpurulent hyperplastic polypoid and cystic degeneration constitutes 28 per cent of the cases.

3. Degeneration of the mucous membrane of the sinuses may be explained in part by the rudimentary microscopic structure of the stroma. A preponderance of loose areolar tissue favors the formation of mesothelial cysts and polypoid degeneration. Membranes of the sinuses endowed with a more fibrous periosteal type of stroma are resistant to the same pathologic processes. The healing power in such a membrane is shown in the case described as it appeared after twenty-five years of mucopurulent sinusitis.

4. Manifest allergic sinusitis occurs in 17 per cent. Nonallergic inflammation of the sinuses as determined by a careful history and examination of the patient and histologic preparations appeared in 47.6 per cent of the cases.

5. The allergic membrane is prone to infection and resistant to treatment. Degenerative changes are greater in allergic sinuses. Hyperplastic sinusitis, especially the

tive changes (abscesses, fibrosis, myxomatous degeneration and so on) is too high. I wonder whether this which we are supposed to accept as allergy might not better be called a characteristic reaction of some people to insult. If this insult is from foreign protein to which they are sensitive, one has manifest allergy. But this reaction may appear to infection or even to chemical insults, and the reason some individuals so react is as yet unknown. At any rate Dr. Semenov's facts show that the rhinologist should not in the presence of this "equivocal allergy" abandon the field. He should study his case more intensively, review the history and every factor involved with meticulous care, and frequently ask for the help of the allergist; but he should not abdicate and should realize that even complete and extensive surgical operation may be necessary in obtaining results. Pathologic classifications cannot be dogmatically applied to individual cases.

DR. RAYMOND O. DART, San Francisco: Dr. Semenov's comprehensive research into the anatomy of the paranasal sinuses is of practical value to the general pathologist. In the aggregate, it is probable that a greater number of rhinologic specimens are examined by general pathologists than by specialists in the field of rhinology. The general pathologist looks to the specialist for the researches which pave the way for him

to make more accurate diagnoses in his routine work. In the available literature on the subject, little is found on the normal anatomy of the paranasal sinuses, and the classifications of the various pathologic processes found in these membranes are varied and confusing. The recognition of allergy as the basic pathologic condition in a large proportion of cases has added to the diagnostic difficulties of the general pathologist. It is not surprising, therefore, to find conflicting reports on the results of the treatment of these cases. Dr. Semenov has defined the limits of the normal anatomy of the paranasal membranes and outlined a workable classification of the various pathologic processes. It is interesting to

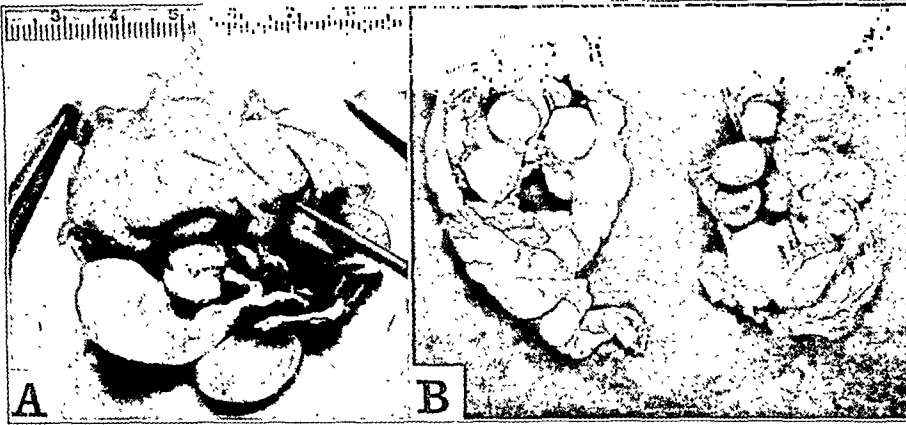


Fig. 10.—A, polyps arising in the antrum attached to the lateral wall and projecting through the ostium into the nasal cavity; B, multiple cystic abscesses in right and left maxillary sinus from a patient with chronic purulent degenerative allergic sinusitis.

bilateral type, is allergic in 70 per cent of the nonpurulent cases.

6. Tissue cultures reveal a preponderance of streptococci and staphylococci in chronic sinusitis, mixed infection being present in 80 per cent.

7. Exudative sinusitis usually responds to conservative treatment. Degenerative changes which are irreversible in character require radical treatment.

8. Postoperative healing in the paranasal cavities is accomplished by the formation of a dense layer of white fibrous connective tissue which epithelizes by an ingrowth of nasal mucosa.

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#### ABSTRACT OF DISCUSSION

DR. ROY F. NELSON, Oakland, Calif.: Pathology is a basic science. I fear I am becoming hypersensitive to the word "allergy." I have a healthy skepticism, doubting whether it is really known what is meant by that word. I know that allergy exists clinically, usually caused by extrinsic foreign proteins and amenable to treatment. However, sometimes "allergy" is used too loosely and has little meaning except "different" or not otherwise understood. Dr. Semenov's classification of "equivocal allergy" is good, but might one not better find some other term altogether? I doubt that eosinophilia and polyposis are necessarily diagnostic of allergy in the accepted clinical sense. Fifty per cent of "equivocal allergic" manifestations in surgical cases is entirely too high. The incidence of frankly degenera-

note that in 35.4 per cent of the author's cases histopathologic conditions suggestive of allergy could not be correlated with clinical history or symptoms. This, together with conflicting reports of other investigators concerning the incidence of allergy and its relation to sinusitis, would indicate that there is need for further and more comprehensive work on this phase of the subject. It is suggested that further studies in this field might be undertaken in a cooperative effort by rhinologists by means of a registry of rhinologic pathology. The splendid results obtained from existing registries are well known. The purpose of most registries has been the study of cancer. Other diseases than cancer might well be made the subject of a comprehensive registry study. A start in this direction was made by the American Academy of Ophthalmology and Otolaryngology when it established the registry for the Section on Laryngology, Otology and Rhinology. Selected cases from this registry were used to prepare the loan sets of otolaryngic pathology now available to members of the academy who are preparing for the examinations of the board. An active registry study of the subject of sinusitis would undoubtedly result in greater understanding of the underlying pathologic principles with consequent improvement in diagnoses and methods of treatment.

**The First State Hospital.**—About 1830 a vigorous movement having for its object the erection of suitable state hospitals for the insane manifested itself simultaneously in several states. This movement found its first concrete expression in Massachusetts with the opening, in 1833, of the State Lunatic Hospital at Worcester.—Deutsch, Albert: *The Mentally Ill in America*, New York, Doubleday, Doran & Co., Inc., 1937.

## Clinical Notes, Suggestions and New Instruments

### EXTREME OBESITY FOLLOWED BY THERAPEUTIC REDUCTION OF TWO HUNDRED AND THIRTY-NINE POUNDS

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The question of how much or at what rate weight may be removed safely is a moot one. From 395½ pounds (180 Kg.), the patient whose case is reported here reached a low weight of 156½ pounds (71 Kg.) in twenty months, with progressive improvement in health throughout the period and subsequently.

#### REPORT OF CASE

L. G., a woman aged 32, Russian, a housewife, applied to the Obesity Clinic for weight reduction on March 22, 1935. She had always been overweight. At 17, when she was married, she weighed 260 pounds (118 Kg.). There had been no change in her mode of living. She considered that her optimum weight



Fig. 1.—Patient when she weighed 402 pounds.

subjectively had been 195 pounds (88.5 Kg.); her maximum weight had been 402 pounds (182.3 Kg.). She slept from eight to ten hours a night, used little tobacco and no alcohol, and had a very good appetite. There were no gastrointestinal symptoms nor any relative to the extremities, such as varicose veins, fallen arches, painful knees or edema. The menses had been irregular since onset, with the exception of the three months just prior to admission, when they followed a twenty-eight day cycle, each period lasting about two and a half days. She had suffered from psoriasis since the age of 8 years.

Her father was of normal weight. Her mother weighed approximately 300 pounds (136 Kg.) and suffered from diabetes. Her brother had weighed 230 pounds (104 Kg.) maximum but at that time weighed 185 pounds (83.9 Kg.). One sister was

obese at 185 pounds. There was no history of hypertension or of cerebral accidents. Two sisters and one brother had died in infancy.

Her height was 63 inches (160 cm.), weight 395½ pounds (the estimated normal was 145 pounds [65.8 Kg.]). The skin showed rather extensive psoriasis, the teeth showed evidence of mild pyorrhea and the tonsils were hypertrophied and cryptic. The arteries were not unduly thickened and the blood pressure was 160 systolic, 120 diastolic. There were a few moist rales at the base of the right lung. The size and contour of the heart were not determined and the abdominal organs were not palpated because of extreme obesity. The physical examination was otherwise essentially negative.

The urine was normal. Dextrose tolerance tests (done by giving the patient 100 Gm. of dextrose in the postabsorptive state) at the fasting and one and two hour periods were respectively 113, 160 and 154 mg. per hundred cubic centimeters of blood March 28, 1935, and 80, 125 and 125 mg. July 14, 1936. At the time of the second dextrose tolerance test, definite hypoglycemic symptoms had become manifest. The urine sugar was negative at all times. Basal metabolic rates are shown in table 1. Blood urea nitrogen was 13.5 mg. and nonprotein nitrogen 32 mg. per hundred cubic centimeters.

This was considered a case of simple obesity, the result of prolonged overnutrition. There were no manifestations to indicate an endocrine etiology.

For treatment she was given a diet, with occasional variations, of approximately 600 calories, which consisted of 35 Gm. of carbohydrate, 70 Gm. of protein and 20 Gm. of fat. Thyroid extract was given in a dose of 3 grains (0.2 Gm.) daily after the second basal metabolism test of April 9, 1936. This was varied from time to time according to indications. The patient followed orders faithfully throughout the entire period from March 22, 1935, to Nov. 17,

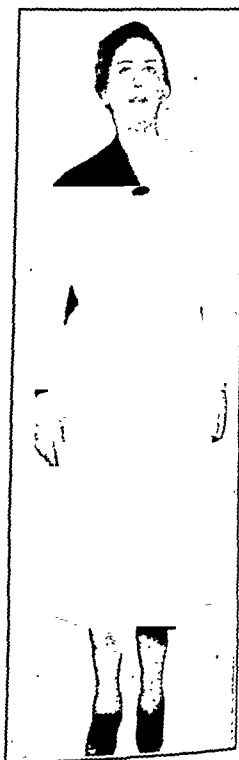


Fig. 2.—After course of treatment when the patient weighed 186½ pounds.

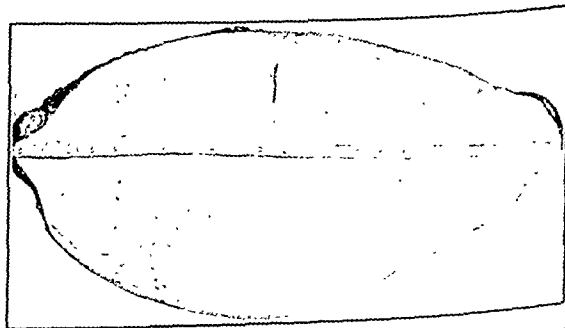


Fig. 3.—Excess skin removed by operation, measuring 24¾ by 12¼ inches.

1936, at which time she weighed 156½ pounds without clothing. A record of her weight losses is shown in figure 4 and table 2.

September 29 she was referred to Dr. Gustave Aufricht of the department of surgery for the removal of excess skin and subcutaneous tissue. At that time her weight was 177½ pounds (80.5 Kg.). Over the abdomen there was a rather large apron

of skin, which was removed by operation October 27 and weighed 5½ pounds (2.5 Kg.). She made a good recovery and was discharged November 17.

## COMMENT

The patient's health remained excellent throughout the entire period of reduction. At no time did she complain of hunger or weakness. There was a moderate improvement in the

TABLE 1.—Metabolism Studies

Date	Weight			Surface Area		Basal Metabolism		Total Heat Production	
	Height, Inches	Pounds	% Above Normal	Square Meters	% Above Normal	Calories Sq.M./hr.	% Above Normal	Calories per Hour	% Above Normal
4/1/35	62.8	397	173.8	2.56	53.2	36.70	+1.6	94.07	+56
4/9/36	63.0	229½	59.5	2.03	20.8	32.27	-10.8	65.51	-7
11/17/36	63.2	156½	8.9	1.72	2.4	32.54	-10.1	55.97	-7

TABLE 2.—Reduction Record of Patient

Date	Weight, Pounds	Blood Pressure	Comment
3/22/35	365½	.....	Diet: calories 600; carbohydrate 33, protein 70, fat 20
5/31/35	357½	154/112	
8/23/35	315½	120/ 50	
10/25/35	292½	.....	
12/27/35	260	122/ 60	Menses regular
3/13/36	237	116/ 94	Feels well
5/23/36	204	128/ 72	Thyroid 3 grains, stopped 6/19/36
7/16/36	188½	106/ 70	Hypoglycemic reaction: diet: calories 900; carbohydrate 100, protein 80, fat 20
8/ 7/36	.....	.....	Diet: Calories 750; carbohydrate 70, protein 75, fat 20
9/25/36	177½	.....	
10/27/36	.....	.....	Plastic operation
11/17/36	156½	.....	Discharged

psoriasis, and the skin showed remarkable adaptability to the smaller proportions. At a weight of 156½ pounds she was in excellent health and spirits, and there was little, when she was clothed, to indicate that she had ever been obese.

During the first months of the reduction period the patient's average loss was 12 pounds (5.4 Kg.) a month. In my experience most patients show an average loss of weight over prolonged periods of 10 pounds (4.5 Kg.) a month.

This case would indicate that there is no limit in the extent to which excess weight may be removed by submaintenance diets, provided such diets contain adequate protein, minerals and vitamins, together with moderate amounts of carbohydrate. Fats may be minimal. To insure sufficient vitamins, these are often added, as such, in concentrated form. Dairy products, such as skim milk and cottage cheese, are valuable in providing adequate calcium and phosphorus. Reductions of from 10 to 20 pounds a month over considerable periods have not been attended by any untoward symptoms in my experience. These observations are entirely in accordance with those of Evans and Strang,<sup>1</sup> who advocate rapid reduction of weight on low calory diets.

An important feature of this case was the high initial total heat production. This, since fat cells themselves are largely inert,<sup>2</sup> in persons who are overweight has the same significance as the "basal" metabolism in those of normal weight and is of far greater importance in indicating the energy exchange of the nonfatty energy-producing tissues of the body.

The figure used to indicate the total heat production is a percentage above or below that which would be produced if the individual were of normal weight (therefore of normal surface area) and had a normal rate of heat production. It is obtained by determining the ideal weight for the individual and from this and the height combined the normal surface area in square meters. This is then multiplied by the calories,

per square meter per hour, that the person should have; i. e., the normal basal metabolism figure. The resultant figure represents the total calories per hour that the person should produce at ideal weight. A comparison with the actual caloric output per hour gives the percentage above or below the normal. This is identical with the current method of expressing the "basal" metabolism, which is also given as a percentage above or below an average normal.

No confusion need be experienced in understanding these two methods of expression if it is remembered that "basal" metabolism relates to heat production under standard conditions per unit of body surface and that total heat production relates to the body as a whole. This important distinction has been too generally ignored. Clinicians have often assumed in the study of overweight that, since the "basal" metabolism is reported normal, the patient's rate of metabolism is also normal. The opposite is actually the case, since the total energy output of the obese is almost invariably too high. The extent to which the metabolism rises depends on the degree of overweight and the consequent increase of surface area. The increase of total heat production, therefore, is in direct proportion to the increase in surface area, provided the "basal" rate remains constant.

In the case under discussion, the total heat production originally was 56 per cent above normal. This might well be compared to a case of normal weight with hyperthyroidism, in which the "basal" metabolism is +56 per cent. Many overweight patients exhibit symptoms similar to hyperthyroidism—hypertension, tachycardia, stimulation of the sympathetic nervous system and diminished dextrose tolerance. This, in my opinion and in that of other observers,<sup>3</sup> can be directly related to the increased metabolism.

The return of the total heat production to normal limits with restoration to ideal weight, as seen in this case, is characteristic. Coincidentally there was a marked subjective improvement throughout the reduction period and an improvement in the dextrose tolerance until symptoms of hypoglycemia were experienced.

To counteract the characteristic decline of the metabolic rate resulting from submaintenance diets (presumably due to a loss of the specific dynamic action of foodstuffs and possibly other factors) I employ thyroid extract in adequate dosage. This dosage has been controlled in a considerable number of cases

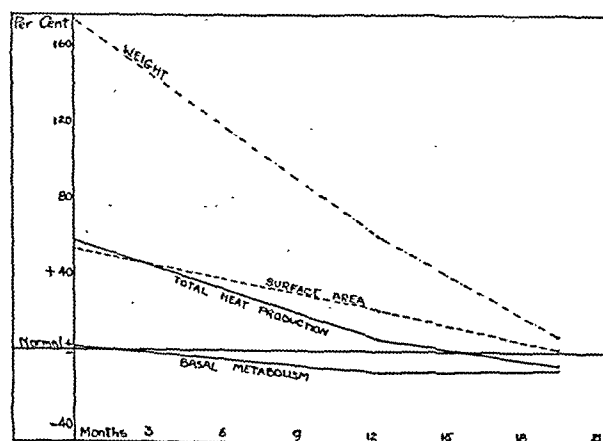


Fig. 4.—Effect of low calory diets and thyroid therapy on weight, surface area, basal metabolism and total heat production.

by repeated determinations of the metabolic rate. Thyroid has been consistently used in the clinic to offset the falling rate of metabolism resulting from reducing diets and to maintain a satisfactory weight loss. Though not well tolerated early for the obvious reason of an increased metabolism, it is well tolerated later, after the effect of the reducing diet has manifested itself.

502 Park Avenue.

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**Special Clinical Article****GASTRIC HEMORRHAGE**

CLINICAL LECTURE AT SAN FRANCISCO SESSION

DAMON B. PFEIFFER, M.D.

PHILADELPHIA

Gastric hemorrhage is a dramatic event. When a person vomits bright red blood or passes a large tarry stool and when in either event he experiences the sickening weakness which accompanies hemorrhage, he usually knows what to do. He calls his doctor. Until a few years ago the doctor, with rare exceptions, thought he also knew what to do. He instituted treatment based on starvation and sedation.

I propose to discuss the problem of gastric hemorrhage from the standpoint of treatment, and as a surgeon I shall confine my discussion to the type of hemorrhage for which the value of surgical intervention is becoming recognized, namely bleeding peptic ulcer. Peptic ulcer, according to Bulmer,<sup>1</sup> causes 89 per cent of acute hemorrhages from the upper part of the intestinal tract, 5.3 per cent of such hemorrhages being caused by esophageal varices and 1.5 per cent by gastric carcinoma. Owen,<sup>2</sup> in studying 137 cases of gross and massive hemorrhage from the intestinal tract at the Philadelphia General Hospital, found that 68 per cent of the hemorrhages were caused by peptic ulcer, 25 per cent by gastric carcinoma and 6 per cent by varices or carcinoma of the esophagus.

That bleeding ulcers give rise to the majority of gastric hemorrhages and hemorrhages from the upper part of the intestinal tract is clear. That the differential diagnosis between peptic ulcer, carcinoma of the stomach, gastritis and the varices of cirrhosis or splenomegaly can be far from simple is perhaps not so well appreciated. It is important, nevertheless, to establish the diagnosis at the earliest possible moment. To discuss differential diagnosis, however, is beside the purpose of this paper.

The problem of treatment arises at once and, like the problem of diagnosis, it is far from simple. Early feeding, as advocated by Meulengracht,<sup>3</sup> the massive drip transfusion<sup>4</sup> and the aluminum hydroxide drip,<sup>5</sup> all relatively recent innovations, suggest that the standard treatment of bleeding peptic ulcer based on starvation and sedation can no longer be universally accepted. Statistical studies go further and show that some patients with bleeding peptic ulcer will die from hemorrhage in spite of any form of medical treatment. Emery and Monroe,<sup>6</sup> reporting on 1,435 cases of peptic ulcer, found that 384 of their patients bled. Of these, twenty, or 5.2 per cent, died of hemorrhage. Allen and Benedict<sup>7</sup> studied 1,804 cases of duodenal ulcer and

found that 30 per cent of the patients bled. Of this number 138 had sudden severe hemorrhages, and for them the mortality was 14.5 per cent. Owen cited a mortality of 6 per cent in 137 cases of gross and massive hemorrhage from peptic ulcer. Twenty-six of his patients had massive hemorrhage from duodenal ulcer and six of these died, giving a mortality of 23 per cent, a figure which emphasizes the danger to life of massive hemorrhage from duodenal ulcer. Bulmer cited a mortality of 10 per cent, Hinton<sup>8</sup> of 11 per cent and Lahey<sup>9</sup> of 5 per cent. In contrast to these figures, Hurst and Ryle<sup>10</sup> reported a mortality from hemorrhage of 3 per cent in private practice and 4.8 per cent in hospital ward practice. Meulengracht reported a mortality of 1.3 per cent with his plan of feeding, his previous mortality with the old regimen of starvation and sedation having been 7.9 per cent. When one analyzes his reports, it would appear that his series is not strictly comparable with the cases of massive hemorrhage with possible surgical implications which are being considered here. His plan cannot yet be recommended.

Such varied mortality rates are puzzling until one remembers that, as Means<sup>11</sup> said, ". . . hemorrhage occurs under a variety of circumstances having different therapeutic significance. There are large exsanguinating hemorrhages; there are small ones carrying little risk. There are first hemorrhages and recurrent hemorrhages. There are hemorrhages in young persons and in old. All these factors have to be taken into consideration in planning treatment."

It seems fair to state that the mortality from massive hemorrhage complicating peptic ulcer, in this country at least, is 5 per cent or more with medical treatment. The mortality from massive hemorrhage complicating duodenal ulcer is definitely higher. The only hope for certain patients lies in early operation.

The attitude of the surgeon toward this complex and interesting problem should be characterized by a desire for close cooperation with the medical man in every case of hemorrhage. Patients should be hospitalized. All efforts should be made to arrive at a prompt and accurate diagnosis. In each case a decision as to whether the patient should be treated medically or whether surgical intervention alone can save him should be made within Finsterer's<sup>12</sup> time limit of from twenty-four to forty-eight hours from the onset of bleeding. The few patients who can be saved only by operation must be operated on early if they are to have every chance.

In making decisions of this nature, one can be guided somewhat by a few established facts. The incidence and the mortality of hemorrhage from ulcer is greater for men than for women. The incidence and the mortality of hemorrhage rise with age and with the presence of arteriosclerosis and hypertension. Hemorrhage from duodenal ulcer carries a higher mortality than hemorrhage from gastric ulcer. Hemorrhage from chronic ulcer is more likely to be fatal than hemorrhage from acute ulcer. Mortality rises rapidly with a second

Read in the Surgical Division of the General Scientific Meetings at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 14, 1933.

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or third massive hemorrhage closely following initial bleeding. According to Gordon-Taylor<sup>13</sup> the mortality from such a second hemorrhage is from 74 to 78 per cent. With regard to patients who survive, Lahey stated that 40 per cent of patients who have bled once will not be relieved of ulcer symptoms by medical treatment and that 80 per cent of patients who have bled two or more times will not be relieved of ulcer symptoms by medical treatment.

TABLE 1.—Incidence of Hemorrhage		
	No. of Cases	Percentage
Total number of cases of ulcer.....	343	..
Perforation.....	81	24
Gross hemorrhage.....	62	18

TABLE 2.—Distribution of Bleeding Ulcers		
	No. of Cases	Percentage
Hemorrhage from duodenal ulcer.....	44	71
Hemorrhage from gastric ulcer.....	15	24
Hemorrhage from anastomotic ulcer.....	3	5

The mortality figures for surgical intervention vary greatly. However, when technic is fairly uniform, the principal factor which influences mortality is the time interval between the onset of hemorrhage and operation. Finsterer has demonstrated that the time element is all important. With thirty-five early resections for massive bleeding he had one death, or a mortality of 2.8 per cent; with forty-two late resections for massive hemorrhage he had thirteen deaths, or a mortality of 31 per cent. Resection is not always possible or necessary. With forty-two early operations of various types, all for severe bleeding, Finsterer had two deaths, or a mortality of 4.8 per cent. He maintained that this is the only fair figure to compare with mortality rates for medical treatment, for early operation means operation within twenty-four to forty-eight hours of the initial bleeding. What is more, this figure must be compared with the mortality for medical treatment in cases of massive hemorrhage and not with the rate for such treatment in general groups of consecutive cases.

The cases I shall report are consecutive cases of severe hemorrhage complicating peptic ulcer which were observed at the Lankenau Hospital during the past four years and at the Abington Memorial Hospital during the past twelve years. Only cases of gross hemorrhage, such as copious hematemesis or melena, frequently associated with syncope and always associated with weakness and a marked fall in the hemoglobin content and red count are included. Four surgeons and twelve medical men handled the patients. While the series is small, it throws some light on the incidence of ulcer complications in private patients and the better class of ward patients.

Table 1 shows the incidence of perforation and gross hemorrhage in all patients admitted during the time covered by this study.

Table 2 shows the distribution of the bleeding ulcers. As in most series, duodenal ulcer was the most frequent site of hemorrhage. Two of the anastomotic ulcers were jejunal, one occurring after a gastroenterostomy performed eleven years previously and the

other after a pylorotomy performed nineteen years previously. The third was gastric, occurring at the site of a sleeve resection done eight years previously.

Table 3 is a comparison of mortality rates with medical and with surgical treatment. The general mortality is 12.9 per cent, the mortality with medical treatment 7.5 per cent and the mortality with surgical treatment 22.7 per cent. Obviously the mortality with operation is higher than it should be. Twelve of the twenty-two operations were on patients who came to operation as medical failures, for whom the surgeon was first called in five or more days after the initial hemorrhage, often after one or more successive hemorrhages, and usually in the face of continued bleeding. Four of these twelve died, and the resulting mortality of 33 per cent represents the mortality for surgically treated medical failures. In the ten cases in which operation was the procedure of election, the only fatality resulted from bundle branch block, which developed on the eighth postoperative day during an otherwise smooth convalescence.

Table 4 is an analysis of the fatalities. The eight patients who died were all men. All but one were over 40. Five had duodenal and three had gastric ulcer. Without more detailed analysis, it may be noted that two fatalities resulted from radical operation for ulcer, two after indirect attack for ulcer and only one when the attack was made directly on the bleeding in the simplest operative fashion. In the last-mentioned case death resulted from bundle branch block after eight days of apparently uncomplicated postoperative recovery.

Table 5 shows the results of a follow-up study of the cases in which treatment was medical. Salient points are the few patients who completely recovered, the number of patients who had symptoms of ulcer and three cases of recurrent bleeding. The patients who

TABLE 3.—Mortality Figures			
	All Patients	Patients Medically Treated	Patients Surgically Treated
Number of patients.....	62	40	22
Deaths.....	8	3	5
Mortality.....	12.9%	7.5%	22.7%

TABLE 4.—Fatalities	
Medical—3	
Hemorrhage .....	duodenal
Hemorrhage .....	gastric
Hemorrhage plus pneumonia.....	duodenal
Surgical—5	
Hemorrhage following excision of ulcer.....	gastric
Hemorrhage following pyloroplasty .....	pyloric
Pneumonia following resection.....	duodenal
Pneumonia following pyloroplasty.....	duodenal
Bundle branch block, heart failure.....	duodenal
Operation: suture at base of ulcer, oversewing of duodenal wall	

bled were men aged 57, 62 and 64, all with duodenal ulcer, and the last of these died of recurrent hematemesis thirteen months after discharge.

Table 6 is a follow-up study of the cases in which treatment was surgical. Points of interest are the high percentage of patients who recovered from all symptoms of ulcer and the two cases of recurrent bleeding. Of the eleven recoveries, six were after pyloroplasty combined with cauterization or suture of the ulcer,

13. Gordon-Taylor, Gordon: The Problem of the Bleeding Peptic Ulcer, Brit. J. Surg. 25: 403 (Oct.) 1937.

three were after posterior gastro-enterostomy and two were after gastric resection. At operation on one of the patients who bled after discharge from the hospital, a large ulcer was found near the common duct complicated by diffuse cholecystitis and chronic catarrhal appendicitis. The gallbladder and appendix were removed in the hope that the ulcer would then subside with medical treatment. Two months after discharge the patient died of hematemesis. This was an early

fusion the beneficial effect of blood is less and said that, if a second transfusion is necessary within forty-eight or seventy-two hours, one should transfuse and operate.

OPERATION

I believe that there are three groups of patients for whom operation is indicated. The first is that group with sudden massive hemorrhage who, according to the criteria just reviewed, are very likely to die with expectant or medical treatment. The second is the group who have severe recurrent bleeding with medical treatment. The third is the group who have recovered from an episode of hemorrhage but who continue to have symptoms of indigestion and high acidity or continued lesser bleeding in spite of medical treatment. Let me emphasize that, with each of these groups, after operation has been performed management along medical lines must continue indefinitely.

If early operation for bleeding is to be done, it should be performed only in cases of definite ulcer. Massive hemorrhage in a man over 50 who is known to have an ulcer and who does not rally soon after the initial hemorrhage is the most obvious indication. With the acute bleeding which occasionally is the first sign of ulcer but may be due to other lesions, the experience and judgment of the medical man and the surgeon conjointly must answer the question. When operation is undertaken, it should be done early, within twenty-four to forty-eight hours after the onset of bleeding, and it should be done with the sole intention of controlling the bleeding directly. By direct attack on the source of bleeding is meant direct localization and exposure of the ulcer, whether gastric or duodenal. At the time of operation one should give massive blood transfusion. In the more fortunate cases immediate resection, which includes the ulcer, may be done without greatly increasing the risk of operation. Surgical judgment is in the highest degree necessary. The important point is to regard the condition as an emergency requiring safe and immediate control of hemorrhage as a complication of ulcer rather than as an ulcer requiring radical operation for its cure. I have previ-

TABLE 6.—Follow-Up After Surgical Treatment (Sixteen of Seventeen Cases, or 92 Per Cent, Traced)

Result	No. of Cases	Percentage	Percentage of Traced Cases	Operation
Complete recovery	11	68	73	Pyloroplasty..... 6 Posterior gastro-enterostomy 3 Gastric resection..... 2
Mild indigestion	1	6	7	Pyloroplasty
Severe indigestion	1	6	7	
Recurrent bleeding	2	12	13	Cholecystectomy, appendectomy, pyloroplasty

ously called attention to the value of anterior gastroduodenotomy in locating the source of hemorrhage at the operating table.<sup>16</sup> The following is a typical case:

CASE 1.—A large duodenal ulcer, almost 1 inch in diameter, was situated on the posterolateral duodenal wall. The patient had had two previous operations without the ulcer's being located. Over a period of eleven years he had bled severely on numerous occasions. The last two almost lethal hemorrhages had occurred within a period of three months. By

TABLE 5.—Follow-Up After Medical Treatment (Twenty-Six of Thirty-Seven Cases, or 70 Per Cent, Traced)

Result	No. of Cases	Percentage	Percentage of Traced Cases
Complete recovery	10	27	39
Mild indigestion	7	18	27
Severe indigestion	5	14	19
Recurrent bleeding	3	8 (1 died)	11
Died, other causes	1	3	4

case, that of a man aged 39, and taught me to attack bleeding ulcers directly. The other patient with recurrent bleeding was a man aged 53 on whom pyloroplasty was performed for pyloric ulcer. Because of the recurrent bleeding, subtotal gastrectomy was advised.

From this series I have learned several lessons. Additional support is given to the fast accumulating evidence that an appreciable number of patients with bleeding ulcer will die of exsanguination with medical treatment alone. Fully realizing that most patients with initial hemorrhage recover with medical treatment, one must realize also that a certain percentage can be saved only by operation. Every patient with severe hematemesis or melena should therefore be hospitalized at once, and on arriving at the hospital the patient should be seen by a medical man and by a surgeon. The diagnosis of ulcer may have been made prior to hemorrhage or may be clear from the history. If not, the necessary and practicable steps should be taken to make it. Unless the bleeding continues unabated, barium sulfate may be given by mouth to aid in diagnosis. The danger in this procedure is not in the giving of the drug but in the transportation of the patient to the x-ray room and in the leaded glove of the examiner. Transportation should be done with care and deep palpation of the abdomen should be forbidden. The patient should be kept recumbent.

Within the first twenty-four hours every effort should be made to judge whether or not the individual is of the group of patients who are not likely to recover with medical treatment. According to Allen and Benedict the eventual survivors pick up rapidly after their first prostration. The prediction as to survival should be based on the severity and duration of bleeding, the patient's reaction to that bleeding, the patient's age and sex and the presence or absence of vascular disturbances. Allen<sup>14</sup> expressed the belief that the age of the patient has more bearing on the cessation of hemorrhage than any other factor, the mortality increasing greatly for patients over 50. The cases just cited indicate that patients between 40 and 50 should also be included in the dangerous group. Jones<sup>15</sup> suggested transfusions as an index to whether or not bleeding will continue. He pointed out that with each trans-

14. Allen, A. W.: Acute Massive Hemorrhage from the Upper Intestinal Tract, *Surgery* 2: 713 (Nov.) 1937.  
15. Jones, D. F., in discussion on Allen and Benedict.

16. Pfeiffer, D. B.: Massive Hemorrhage from Posterior Duodenal Ulcer, *Ann. Surg.* 103: 473 (March) 1936.

gastroduodenotomy a low posterior ulcer was found, an exposed vessel in the bed was sealed by electrocautery, the bed was cauterized, the craggy edges were nicked circumferentially and the operation completed as a wide pyloroplasty. The patient made an uncomplicated recovery and was free from bleeding or symptoms of ulcer four years later.

I repeat that, as a rule, I believe that the bleeding patient should not be subjected to too much surgical procedure. While the ulcer is bleeding is the time for the saving of life, not for the curing of the ulcer. The situation is somewhat similar to that in which operation is performed for intestinal obstruction due to colonic growths when obstruction is relieved at primary operation and the growth is later removed. The objective in the cases under discussion is hemostasis. Gastrotomy or duodenotomy will usually provide access to the ulcer. In the ulcer bed the actual bleeding point can frequently be found. The point may be sealed with the ball electrode, and an encircling stitch of chromic catgut may be placed through the tissues above and below. If the point is not discovered, similar procedures may still be adopted and it may be possible to mobilize overhanging edges and bring them together by suture. Small radiating incisions may be of advantage in the case of a large excavated ulcer. It is impossible to enumerate the precise procedures adapted to the varying individual cases, but it is important that uppermost in the surgeon's mind should be the immediate objective of controlling hemorrhage and not the ultimate desideratum of cure of the ulcer. A great advantage of anterior gastroduodenotomy for posterior ulcer is the opportunity afforded by it to terminate the operation as a gastroduodenostomy. While this procedure is not recommended as a definitely curative operation for ulcer, it would seem to be that in many instances. The mortality with such a procedure is extremely low. It may be done without exceeding the vitality of an exsanguinated patient, and it does not interfere with a subsequent radical operation should that be considered wise.

A case illustrative of these principles was observed at the Abington Memorial Hospital three weeks ago, too late to be included in the statistics just presented:

CASE 2.—A man aged 50, who had epigastric pain and vomiting characteristic of peptic ulcer for several days, in 1919 had a posterior gastro-enterostomy at another hospital for duodenal ulcer. The morning of admission he passed a large tarry stool, and he was admitted to the hospital in a state of shock. He rallied fairly well, but the next morning he vomited a large amount of bright red blood and again went into shock. The blood pressure fell to 80/30. The hemoglobin content was 55 per cent and the red count 3,200,000. Operation with massive transfusion was performed a few hours later. A gastrotomy gave ready access to a gastrojejunal ulcer with an open vessel in the bed. The ulcer was partially excised within the stomach and bleeding was stopped. The patient's convalescence has been perfectly smooth.

In cases in which bleeding has been controlled with medical treatment, operation must be considered because of the likelihood of another hemorrhage in the future. Here judgment is essential. Recurrent bleeding with medical treatment indicates progression of the ulcer, and operation should be performed. Subtotal gastrectomy with removal of the ulcer is usually the best curative procedure.

When bleeding has been controlled by medical measures but pain due to ulcer and high acidity persist in spite of treatment, resection should also be considered.

#### CONCLUSION

The treatment of gastric hemorrhage caused by a bleeding peptic ulcer is a complicated problem which calls for the pooled resources and close cooperation of the medical man and the surgeon.

A certain number of patients with bleeding ulcer will die with medical treatment. Every effort should be made to single these patients out and to give them the benefit of early operation.

At operation for bleeding ulcer, the primary consideration is hemostasis. After operation continued medical care should be the rule, and in selected cases more extensive surgical procedure should be considered.

1822 Pine Street.

### Council on Pharmacy and Chemistry

#### ERGONOVINE

##### Report of the Council on Pharmacy and Chemistry

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT, WHICH HAS KINDLY BEEN PREPARED FOR THE COUNCIL BY DR. RALPH G. SMITH.

PAUL NICHOLAS LEECH, Secretary.

#### THE PRESENT STATUS OF ERGONOVINE

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The recent discovery of a new and pharmacologically potent alkaloid of ergot has aroused considerable interest both in purely scientific and in clinical circles. Certain factors which have stimulated such interest are as follows: It is characterized by a number of physical, chemical and pharmacologic properties which differ decidedly from those of the previously known alkaloids of ergot, all of which show considerable similarity. Although hitherto unrecognized, it apparently plays an important role in the clinical oxytocic activity of those preparations of ergot which contain it and in the purified form is proving itself to be a valuable drug in the practice of obstetrics. Furthermore, the closely consecutive publications of its discovery from various laboratories naturally initiated discussion regarding priority.

As sufficient time has elapsed since the first announcements for general agreement on the properties of the alkaloid and for some indication of its therapeutic application, it is possible to describe its characteristics with a minimum of controversial discussion. However, before proceeding to that phase of the subject it might be of interest to review briefly the publications concerned with its early development.

Chassar Moir<sup>1</sup> in 1932, by means of the intra-uterine rubber bag method of Bourne and Burn,<sup>2</sup> recorded uterine contractions and tonus changes following the administration of various ergot preparations to puerperal patients. Several samples of B. P. liquid extracts

From the Laboratory of Pharmacology, University of Michigan Medical School.

1. Moir, Chassar: The Action of Ergot Preparations on the Puerperal Uterus. *Brit. M. J.* 1: 1119-1122 (June 18) 1932.

2. Bourne, Alceck, and Burn, J. H.: The Dosage and Action of Pituitary Extract and of the Ergot Alkaloids on the Uterus in Labor, with a Note on the Action of Adrenalin. *J. Obst. & Gynaec. Brit. Emp.* 34: 249-268, 1927.

of ergot, prepared by aqueous extraction and containing only traces of the known ergot alkaloids, invariably produced, in 2 drachm (7.5 cc.) doses, a decided response which was more marked, especially with regard to tonus increases, than that produced by pure ergotoxine or ergotamine preparations administered by mouth or even by intramuscular injection. It having also been demonstrated that the activity of the liquid extracts could not be explained by their histamine or tyramine content, the action was ascribed to some still unknown factor.

Swanson and Hargreaves<sup>3</sup> in 1934 reported the comparative effect, as recorded by an intra-uterine rubber balloon, of various ergot preparations on the intact puerperal uteri of etherized dogs. On oral administration certain extracts and fluidextracts of ergot produced a definite response in from four to twenty minutes, while comparable doses, as determined by the cock's comb assay method, of ergotamine tartrate and ergotoxine ethanesulfonate brought about a similar effect only in from thirty to sixty minutes. Little difference in the various preparations was detected on intravenous administration. The conclusion reached was that "ergot contains a principle (not ergotamine or ergotoxine) that produces by mouth a rapid onset of action on the puerperal uterus of dogs."

Early in 1935 certain papers appeared from various sources which confirmed and extended these observations. Thompson<sup>4</sup> in January and March reported a study of various ergot preparations and fractions as recorded from the exposed uterus of the lightly anesthetized pregnant cat. (The two papers were previously presented at meetings of the American Pharmaceutical Association in August 1932 and May 1934 respectively.) According to the January report, hydro-alcoholic and aqueous extracts of ergot were prepared, containing the alkaloidal equivalent in 1 cc. of 0.5 mg. and 0.19 mg. respectively of ergotoxine ethanesulfonate as assayed by the Broom-Clark and cock's comb methods. These extracts produced a similar response, usually within ten minutes, in contrast to equivalent amounts of ergotoxine and ergotamine salts, which were more weakly effective and only in from thirty to sixty minutes after oral administration. Such results confirmed the work of Moir, suggesting the presence of some unknown potent principle which was considered as alkaloidal in nature. In the March paper were reported the method of separation of the new active substance in an amorphous form and certain of its properties, its smaller molecule and its greater solubility in water and numerous organic solvents in comparison with other ergot alkaloids being recognized. From the pharmacologic description, a very crude preparation was obviously concerned but a footnote reported its isolation in crystalline form. Thompson<sup>5</sup> later stated that the footnote was in the paper at the time of its submission for publication in May 1934 and in his doctorate dissertation, submitted before that time; also that the isolation in crystalline form was reported at the American Pharmaceutical Association meetings in May 1934 and that in the same month the name "ergostetrine" was assigned in a U. S. patent application. In a paper

delivered in April 1935 at a meeting of the American Society for Pharmacology and Experimental Therapeutics the alkaloid was referred to as ergostetrine, but in an abstract<sup>6</sup> of this paper published in June 1935 it is still called "X" alkaloid. The method of isolation appeared in September 1935.<sup>7</sup> Koff<sup>8</sup> reported in February 1935 a clinical investigation of ergot preparations by the intra-uterine balloon method, confirming Moir's conclusions regarding an unknown active substance in ergot. Also, on examination of Thompson's extracts he found the activity to lie wholly in the alkaloidal fraction, which still showed similar effects after removal of the ergotoxine group of alkaloids.

A publication by Davis, Adair, Rogers, Kharasch and Legault<sup>9</sup> appeared in February 1935 (previously presented at a meeting of the Central Association of Obstetricians and Gynecologists in November 1934) reporting the extraction of a water and alcohol soluble fraction from ergot which was considered to be non-alkaloidal on the basis of certain properties not characteristic of the known ergot alkaloids. This fraction in 3 mg. doses by mouth in more than 100 cases produced an increase in rhythm and tone in the quiescent puerperal uterus, beginning in fifteen minutes and persisting for from three to four hours after administration, as recorded by the intra-uterine balloon method. On the contrary, ergotamine, ergotoxine and sensibamine (now believed to be an equimolecular combination of ergotamine and ergotaminine<sup>10</sup>) in 3 mg. doses by mouth produced no effect over a period of one hour. The experiments here described were carried out with an impure substance, but in a footnote it was stated that the active principle had been isolated in crystalline form. In another footnote it was reported that a commercial firm had consented to make large quantities of the substance for clinical assay and had given it the name "ergotocin." The impression is given that "ergotocin" referred to the impure product, but Kharasch and Legault later state, in publications describing certain properties and clinical effects of the pure substance, that it referred to the crystalline product which had been obtained in December 1934<sup>11</sup> and which Eli Lilly & Co. had been preparing for two months and with which they had records on more than 200 patients.<sup>12</sup> A photomicrograph of the needle-shaped crystals of ergotocin, isolated by Kharasch, appeared on the cover of the March 1935 *Journal of Chemical Education*.<sup>13</sup> The empirical formula  $C_{21}H_{27}O_3N_3$  (which included a molecule of ethyl alcohol), assigned to the alkaloid by Kharasch and Legault, was published in June 1935.<sup>14</sup> The study of the chemistry of ergot was apparently begun by Kharasch and Legault early in 1932.<sup>15</sup>

6. Thompson, Marvin R.: The Active Principles of Ergot, *J. Pharmacol. & Exper. Therap.* **54**: 161 (June) 1935.

7. Thompson, Marvin R.: Some Properties of Ergostetrine, *J. Am. Pharm. A.* **24**: 748, 1935.

8. Koff, Arthur K.: A Study of the Action of Ergot on the Human Puerperal Uterus, *Surg., Gynec. & Obst.* **60**: 190 (Feb.) 1935.

9. Davis, M. E.; Adair, Fred L.; Rogers, Gerald; Kharasch, M. S., and Legault, Romeo R.: A New Active Principle in Ergot and Its Effect on Uterine Motility, *Am. J. Obst. & Gynec.* **29**: 155-167 (Feb.) 1935.

10. Stoll, Arthur; Rothlin, E.; Löffler, W., and Dale, Sir Henry: Die Pharmakologie des Mutterkorns, *Schweiz. med. Wchnschr.* **65**: 1077-1082 (Nov. 9) 1935.

11. Kharasch, M. S., and Legault, R. R.: Ergotocin, *Science* **81**: 353 (April 19) 1935. Ergotocin: The Active Principle of Ergot Responsible for the Oral Effectiveness of Some Ergot Preparations on Human Uteri, *J. Am. Chem. Soc.* **57**: 956 (May) 1935.

12. Kharasch, M. S., and Legault, R. R.: Ergotocin, *Lancet* **1**: 1243 (May 25) 1935; footnote 14, first reference.

13. The explanation appeared in the May issue, p. 238.

14. Kharasch, M. S., and Legault, R. R.: The New Active Principle of Ergot, *Science* **81**: 614-615 (June 21) 1935; footnote 44, first reference.

15. Adair, Fred L.; Davis, M. E.; Kharasch, M. S., and Legault, R. R.: A Study of a New and Potent Ergot Derivative (Ergotocin), *Am. J. Obst. & Gynec.* **30**: 466 (Oct.) 1935; **30**: 740 (Nov.) 1935.

3. Swanson, Edward E., and Hargreaves, Chester C.: The Action of Ergot and Its Alkaloids on the Puerperal Uteri of Dogs, *J. Am. Pharm. A.* **23**: 867, 1934.

4. Thompson, Marvin R.: The Active Constituents of Ergot: A Pharmacological and Chemical Study, *J. Am. Pharm. A.* **24**: 24-38 (Jan.), 185-196 (March) 1935.

5. Thompson, Marvin R.: The New Active Principle of Ergot, *Science* **81**: 636-639 (June 28) 1935.

The first detailed description of the method of preparation, physical properties and results of chemical analysis of the crystalline form of the new alkaloid, which they named "ergometrine" was published by Dudley and Moir<sup>16</sup> in March 1935. The analytic results were presented with reservation to allow slight modification after more drastic purification and no empirical formula was suggested at this time. Some modification of the analytic results and also of the physical properties was later found to be necessary. In the same paper, clinical results as recorded by the intra-uterine bag method and also by extra-abdominal recording apparatus were presented showing stronger and more prompt uterine activity on administration of the new alkaloid by mouth, intramuscularly or intravenously than that produced by the previously known ergot alkaloids. The former was also free from undesirable side actions. Some of the pharmacologic observations of Brown and Dale, such as the practical absence of epinephrine inhibiting effect, were included. The description of a method of preparation suitable for large scale operation was published later.<sup>17</sup>

In May 1935 Stoll and Burckhardt<sup>18</sup> reported the isolation in crystalline form of a new ergot alkaloid which they named "ergobasin" (referring to its comparatively strong basic reaction in aqueous solution), described the method of preparation and certain of its physical and chemical properties and presented photomicrographs of the crystals of the alkaloid and of certain of its salts. (It was later stated<sup>10</sup> that ergobasine had been prepared at the beginning of 1935.) On the basis of their analyses the empirical formula was announced as  $C_{19}H_{23}O_2N_3$ , which was confirmed by Jacobs and Craig,<sup>19</sup> who reported in July 1935 the isolation of the same alkaloid. The same formula was later accepted by Dudley,<sup>20</sup> by Davis, Adair and Pearl<sup>21</sup> and by Thompson.<sup>7</sup>

As a result of this contemporaneous work and the announcement in close succession of the isolation of the new alkaloid by four laboratories in Europe and America, considerable discussion naturally arose regarding priority.<sup>22</sup> At least a part of the confusion resulted from the uncertainty that all workers had isolated the same principle, since the initial announcements concerned preparations not absolutely pure and consequently differing slightly in physical constants and chemical properties. An exchange of samples among the four laboratories resulted in a mutual publication early in 1936 by Kharasch, King (in place of Dudley, then deceased), Stoll and Thompson<sup>23</sup> to the effect that ergometrine, ergotocin, ergobasin and ergostetrine were the same substance and that the four names were

synonymous. A detailed report of the comparison as carried out by Stoll and Burckhardt was later published.<sup>24</sup> Chen, Swanson, Kleiderer and Clowes<sup>25</sup> in a comparison involving action on the isolated rabbit uterus, the cock's comb and the *p*-dimethylamino benzaldehyde reactions and combustion analyses reached the same conclusion. Thompson<sup>26</sup> also reported identity on the basis of physical and pharmacologic characteristics.

On March 14, 1936, the Council on Pharmacy and Chemistry of the American Medical Association adopted the name "ergonovine" for the new ergot alkaloid,<sup>27</sup> since all of the names mentioned were either considered therapeutically suggestive (ergotocin, ergostetrine, ergometrine) or were proprietary (ergotocin, ergostetrine, ergobasin). Although the Council concedes to the discoverer the right to a proprietary name, in order to avoid confusion it is the policy to recognize only one such name for the same substance. In this case it was unable to establish undisputed priority so decided to allow no proprietary name. The action of the Council stimulated certain adverse criticism.<sup>28</sup> The names "ergometrine" and "ergobasin" are still being used in Europe.

Regarding priority, it is of interest that on June 13, 1932, about one week before the appearance of Moir's early paper,<sup>1</sup> Elmer H. Stuart of the Eli Lilly Company made U. S. patent application for an ergot-derived product and a process for obtaining it. This product was conceded to be a mixture but from its peculiar optical rotation ( $[\alpha]_D^{25} = -34^\circ$ ) in chloroform it was argued that it contained an alkaloid not hitherto described, in addition to ergotoxine and ergotamine, and having similar physiologic properties. In an amendment filed March 24, 1933, the high potency on the puerperal uterus in comparison to ergotamine and ergotoxine was stressed. From time to time patent claims were extended to cover properties as they were discovered, mostly by other investigators, which were confirmed for this mixture or for ergonovine separated from it. A patent covering all these properties was finally granted, Jan. 12, 1937. However, the Council on Pharmacy and Chemistry refused the claim, on the basis of this patent, of the Eli Lilly Company to the right of a proprietary name for the purified alkaloid, in that Stuart was not the first one to isolate it or to distinguish clearly its most important medical properties.

#### PHYSICAL AND CHEMICAL PROPERTIES

The alkaloidal base ergonovine is a colorless, tasteless, odorless, crystalline substance, appreciably soluble in water (1:200-300 at 20 C.<sup>18</sup>), showing in solution a weak but definitely alkaline reaction<sup>29</sup> and a bluish fluorescence.<sup>30</sup> In dilute aqueous solutions of organic and mineral acids it dissolves very readily.<sup>31</sup> It is freely

16. Dudley, H. W., and Moir, Chassar: The Substance Responsible for the Traditional Clinical Effect of Ergot, *Brit. M. J.* **1**: 520 (March 16) 1935.

17. Dudley, Harold W.: The Preparation of Ergometrine, *Pharmaceut. J.* **134**: 709 (June 15) 1935.

18. Stoll, Arthur, and Burckhardt, Ernst: L'ergobasine, un nouvel alcaloïde de l'ergot de seigle soluble dans l'eau, *Compt. rend. Acad. d. sc.* **200**: 1680-1682 (May 13) 1935; *Bull. d. sc. pharmacol.* **42**: 257-266 (May) 1935.

19. Jacobs, Walter A., and Craig, Lyman C.: On an Alkaloid from Ergot, *Science* **82**: 16-17 (July 5) 1935.

20. Dudley, H. W.: The Relationship of Ergotocin to Ergometrine, *J. Am. Chem. Soc.* **57**: 2009 (Oct.) 1935; footnote 33.

21. Davis, M. Edward; Adair, Fred L., and Pearl, Sarah: The Present Status of Oxytocics in Obstetrics, *J. A. M. A.* **107**: 261-267 (July 25) 1936.

22. Dale, H. H.: The New Ergot Alkaloid, *Science* **82**: 99-101 (Aug. 2) 1935. Stoll, Arthur: The New Ergot Alkaloid, *Ibid.* **82**: 415-417 (Nov. 1) 1935. Thompson,<sup>7</sup> Kharasch and Legault, footnote 14, first reference. Dudley and Moir,<sup>16</sup> The Active Oxytocic Principle of Ergot, editorial, *J. A. M. A.* **104**: 1910 (May 25) 1935. The Relationship of the Recently Discovered Ergot Alkaloids.<sup>6</sup>

23. Kharasch, M. S.; King, H.; Stoll, A., and Thompson, Marvin R.: The New Ergot Alkaloid, *Science* **83**: 206-207 (Feb. 28) 1936; *Nature* **137**: 403, 1936; *Schweiz. med. Wchnschr.* **66**: 261 (March 14) 1936.

24. Stoll, Arthur, and Burckhardt, Ernst: Das neue Mutterkornalkaloid, *Schweiz. med. Wchnschr.* **66**: 353-354 (April 11) 1936.

25. Chen, K. K.; Swanson, Edward E.; Kleiderer, E. C., and Clowes, G. H. A.: Ergotocin, Ergometrine, Ergostetrine and Ergobasine, *J. Pharmacol. & Exper. Therap.* **57**: 74 (May) 1936.

26. Thompson, Marvin R.: Some Observations on the Pharmacology of Ergostetrine (Ergometrine, Ergobasine, Ergotocin), *J. Pharmacol. & Exper. Therap.* **57**: 145 (June) 1936.

27. The New Ergot Alkaloid "Ergonovine," Report of the Council on Pharmacy and Chemistry of the American Medical Association on the New Ergot Alkaloid, *J. A. M. A.* **106**: 1008 (March 21) 1936; *Science* **83**: 296-297 (March 27) 1936; Ergonovine, Current Comment, *J. A. M. A.* **106**: 1012-1013 (March 21) 1936.

28. Why Ergonovine? *Pharmaceut. J.* **136**: 397 (April 11) 1936. Council Correspondence with Sir Henry Dale, *J. A. M. A.* **108**: 1969-1971 (June 5) 1937. Stoll.<sup>11</sup>

29. Dudley and Moir.<sup>16</sup> Dudley.<sup>22</sup> Kharasch and Legault.<sup>14</sup> Stoll and Burckhardt.<sup>18</sup> Thompson.<sup>7</sup>

30. Dudley.<sup>22</sup> Stoll and Burckhardt.<sup>18</sup> Thompson.<sup>7</sup> Allport and Crews.<sup>34</sup> 31. Adair, Davis, Kharasch and Legault.<sup>15</sup> Kharasch and Legault.<sup>14</sup> Thompson.<sup>7</sup>



soluble in methyl and ethyl alcohol,<sup>32</sup> ethyl acetate, acetone, methyl ethyl ketone,<sup>33</sup> acetic ether,<sup>18</sup> less so in ether<sup>15</sup> and sparingly soluble in dichlorethylene,<sup>33</sup> benzene<sup>34</sup> and especially in chloroform.<sup>35</sup>

Ergonovine may be crystallized from a number of solvents, possibly most readily from benzene and chloroform, appearing in the form of long fine needles.<sup>36</sup> Characteristic crystallizations from other solvents have also been described.<sup>37</sup> A troublesome characteristic of ergonovine is a tendency for the crystals to retain some of the solvent in their formation and to release it only with comparatively drastic treatment.<sup>38</sup> This phenomenon apparently accounted for the erroneous empirical formula originally assigned by Kharasch and Legault, an equivalent of alcohol being retained in their preparation.<sup>39</sup>

A melting point with decomposition of 159-163 C. includes most of the values reported for the purified product,<sup>40</sup> although one as high as 164 C.<sup>54</sup> has been obtained. The optical activity, including specific rotation values [e.g.  $[\alpha]_D^{23} = +86^\circ$  ( $c = 0.199$ ) in water,<sup>24</sup>  $[\alpha]_D^{25} = -44^\circ$  ( $c = 0.08$ ) in chloroform<sup>41</sup>] which have been used extensively for identification purposes, has been described in numerous publications.<sup>42</sup>

In contrast to the other alkaloids which are precipitated in dilutions of from 1:200,000 to 1:2,000,000 by Mayer's reagent, ergonovine is not precipitated in dilutions above 1:5,000-1:10,000.<sup>43</sup>

A variety of crystalline salts have been prepared<sup>44</sup> and their characteristic crystal forms described.<sup>45</sup> The melting points<sup>46</sup> and optical activities have been reported for several of them, all preparations showing dextrorotation.<sup>47</sup> The water solubility of the salts is also high in comparison with other alkaloids of ergot, the maleate being soluble in water to the extent of 2 per cent at 38 C.<sup>18</sup>

Certain observations have been made regarding the stability of various preparations. Although aqueous solutions of the base are slowly oxidized on exposure to air, acquiring a brown color,<sup>49</sup> solutions in dilute polybasic aliphatic organic acids are stable at ordinary

temperatures and may be sterilized by boiling at 100 C. without appreciable loss in oxytocic activity and without imparting color to the solution.<sup>15</sup> The salts keep well in the dry state<sup>21</sup> or in solution in ampules,<sup>50</sup> although the heating of solutions of the salts in sealed tubes for any length of time results in decomposition and darkening.<sup>21</sup>

With regard to color tests characteristic of other ergot alkaloids and dependent on the indole nucleus, ergonovine gives positive glyoxylic acid, Keller and *p*-dimethylaminobenzaldehyde reactions.<sup>51</sup> The last reagent, used in the M. I. Smith colorimetric assay method, yields a more intense color with ergonovine than with the ergotoxine-ergotamine group when compared on a weight basis,<sup>52</sup> in keeping with the smaller molecular weight of ergonovine. Hampshire and Page<sup>53</sup> have obtained equivalent results with ergotoxine and ergonovine when compared on a molecular basis. The color produced by ergonovine in this reaction is spectroscopically identical with that produced by ergotoxine under the same conditions.<sup>54</sup> A positive color reaction has also been reported with the Folin-Denis phenol reagent.<sup>55</sup>

As already indicated, ergonovine,  $C_{19}H_{23}N_3O_2$ , has a definitely smaller molecule than ergotoxine,  $C_{35}H_{50}O_5N_5$ , and other alkaloids of ergot with the exception of ergomonamine.<sup>56</sup> On alkaline hydrolysis, it resembles the other alkaloids in yielding lysergic acid<sup>57</sup> but differs from them in the remaining part of the molecule. In the case of ergonovine this consists of a single and comparatively simple radicle *d*-2-amino propanol-1 ( $CH_3-CH.NH_2-CH_2.OH$ ).<sup>58</sup>

It is of interest that Smith and Timmis<sup>59</sup> have isolated from ergot and described the properties of an isomer of ergonovine (ergometrine) which they have named ergometrinine. This has been confirmed by Stoll,<sup>60</sup> ergobasinin. This alkaloid, in its physical properties, more closely resembles the older group of ergot alkaloids than does ergonovine. By suitable treatment these two alkaloids are interconvertible and constitute a pair of isomers corresponding to the pairs of previously known alkaloids ergotoxine ergotinine, ergotamine ergotaminine and the still more recently isolated ergosine ergosinine<sup>61</sup> and ergocristine ergocristinine.<sup>62</sup>

32. Dudley.<sup>23</sup> Stoll and Burekhardt.<sup>18</sup> Thompson.<sup>7</sup> Adair, Davis, Kharasch and Legault.<sup>25</sup>

33. Dudley, Harold W.: Ergometrine, Proc. Roy. Soc., London, s. B. **118**: 478-484 (Oct. 3) 1935.

34. Dudley.<sup>23</sup> Thompson.<sup>7</sup> Adair, Davis, Kharasch and Legault.<sup>25</sup>

35. Stoll and Burekhardt.<sup>18</sup> Thompson.<sup>7</sup> Dudley.<sup>23</sup>

36. Adair, Davis, Kharasch and Legault.<sup>25</sup> Davis, Adair and Pearl.<sup>21</sup>

Dudley and Moir.<sup>16</sup> Dudley.<sup>23</sup> Stoll and Burekhardt.<sup>18</sup> Thompson.<sup>7</sup>

37. Dudley, H. W.: Properties of Ergometrine, Brit. M. J. **1**: 798 (April 13) 1935. Grant, R. L., and Smith, S.: Dimorphism of Ergometrine, Nature **137**: 154, 1936; Pharmaceut. J. **136**: 146 (Feb. 8) 1936. Dudley and Moir.<sup>16</sup> Stoll and Burekhardt.<sup>18</sup> Dudley.<sup>23</sup> Stoll.<sup>60</sup>

38. Stoll and Burekhardt.<sup>18</sup> Dudley.<sup>23</sup>

39. Davis, Adair and Pearl.<sup>21</sup> Jacobs and Craig.<sup>19</sup>

40. Thompson, Marvin R.: The New Active Principle of Ergot, Science **82**: 62-63 (July 19) 1935. Kleiderer, E. C.: Optical Rotation Study of the New Orally Effective Principle of Ergot, J. Am. Chem. Soc. **57**: 2007 (Oct.) 1935. Adair, Davis, Kharasch and Legault.<sup>25</sup> Dudley.<sup>23</sup> Stoll and Burekhardt.<sup>18</sup> Dudley.<sup>23</sup>

41. Stoll, Arthur: Les alcaloïdes de l'ergot de Seigle, Bull. d. sc. pharmacol. **43**: 465-490 (Aug.-Sept.) 1936; Die Alkaloïde des Mutterkorns, Wien, klin. Wchnschr. **49**: 1513-1517 (Dec. 11) 1935-1936 (Dec. 18) 1936.

42. Smith, Sydney, and Timmis, Geoffrey Millward: The Alkaloids of Ergot: Part VII. Isoergine and Isohysergic Acids, J. Chem. Soc., 1936, p. 1440. Bennekou, I., and Schou, Svend A.: Optical Behavior of Ergometrine, Dansk. tids. farm. **10**: 105-108, 1936; Chem. Abstr. **30**: 3944, 1936. Dudley.<sup>23</sup> Stoll and Burekhardt.<sup>18</sup> Jacobs and Craig.<sup>19</sup>

43. Stoll.<sup>60</sup> Kleiderer.<sup>40</sup> Kharasch and Legault, footnote 14, second reference. Adair, Davis, Kharasch and Legault.<sup>25</sup>

44. Stoll and Burekhardt.<sup>18</sup> Kharasch and Legault.<sup>25</sup> Adair, Davis, Kharasch and Legault.<sup>25</sup> Davis, Adair and Pearl.<sup>21</sup>

45. Kharasch, M. S., and Legault, R. R.: Ergotocin, J. Am. Chem. Soc. **57**: 1140 (June) 1935. Dudley.<sup>23</sup> Davis, Adair, Chen and Swanson.<sup>48</sup>

46. Kleiderer.<sup>40</sup> Stoll.<sup>60</sup> Stoll and Burekhardt.<sup>18</sup> Kharasch and Legault.<sup>25</sup>

47. Chen, Swanson, Kleiderer and Clowes.<sup>27</sup> Dudley.<sup>23</sup>

48. Stoll and Burekhardt.<sup>18</sup> Stoll.<sup>60</sup> Kharasch and Legault.<sup>25</sup> Dudley.<sup>23</sup>

49. Dudley.<sup>23</sup> Kharasch and Legault.<sup>25</sup> Kleiderer.<sup>40</sup>

50. Dudley.<sup>23</sup> Stoll and Burekhardt.<sup>18</sup> Kleiderer.<sup>40</sup>

51. Davis, M. Edward; Adair, Fred L.; Chen, K. K., and Swanson, Edward E.: The Pharmacological Action of Ergotocin, a New Ergot Principle, J. Pharmacol. & Exper. Therap. **54**: 398-407 (Aug.) 1935.

52. Dudley and Moir.<sup>16</sup> Dudley.<sup>23</sup> Stoll and Burekhardt.<sup>18</sup>

53. Moir, Chassar: Clinical Experiences with the New Alkaloid (Ergometrine), Brit. M. J. **2**: 799-801 (Oct. 24) 1936; Ergometrine, ibid. **2**: 243 (Aug. 1) 1936.

54. Dudley, Harold W., and Moir, Chassar: The New Active Principle of Ergot, Science **81**: 559-560 (June 7) 1935. Austoni, Mario: Methods and Results Obtained in the Determination of Alkaloids of Seigle Cornutum, Bol. Soc. ital. sper. **10**: 643-647, 1935. Jacobs and Craig.<sup>19</sup>

55. Dudley.<sup>23</sup> Thompson.<sup>7</sup> Kharasch and Legault.<sup>25</sup> Stoll and Burekhardt.<sup>18</sup>

56. Allport and Crews.<sup>54</sup> Hampshire and Page.<sup>53</sup> Stoll and Burekhardt.<sup>18</sup> Kharasch and Legault.<sup>25</sup> Thompson.<sup>7</sup>

57. Hampshire, C. H., and Page, G. R.: The Chemical Assay of Ergot, Quart. J. Pharm. & Pharmacol. **9**: 60 (No. 1) 1936.

58. Allport, Noel L., and Crews, Sydney K.: Spectrographic Absorption of Ergometrine in Relation to the British Pharmacopoeia Color Test, Quart. J. Pharm. & Pharmacol. **8**: 447-452, 1935; Pharmaceut. J. **135**: 8 (July 6) 1935.

59. Kharasch and Legault.<sup>25</sup> Adair, Davis, Kharasch and Legault.<sup>25</sup>

60. Holden, G. W., and Diver, G. R.: A New Alkaloid and an Acid Salt from Ergot, and an Acid Derived from the Salt, Quart. J. Pharm. & Pharmacol. **9**: 230-234 (No. 2) 1936.

61. Jacobs and Craig.<sup>19</sup> Kharasch and Legault.<sup>25</sup>

62. Kharasch, M. S.; Stanger, D. W.; Bloodgood, M. A., and Legault, R. R.: Spectroscopic Similarity Between Ergot (Lysergic Acid) and the Yohimbine Alkaloids, Science **83**: 36-38 (Jan. 10) 1936. Jacobs and Craig.<sup>19</sup>

63. Smith, Sydney, and Timmis, Geoffrey Millward: A New Alkaloid of Ergot, Nature **136**: 259, 1935; Ergometrinine, Pharmaceut. J. **135**: 212 (Aug. 24) 1935; The Alkaloids of Ergot: Part VI, Ergometrinine, J. Chem. Soc. **1166**, 1936.

64. Stoll, Arthur: Ergobasine and Its Relation to the Alkaloids of the Ergotamine-Ergotoxine Group, München. med. Wchnschr. **84**: 322-324 (Feb. 26) 1937; footnote 41.

65. Smith, Sydney, and Timmis, Geoffrey Millward: A New Alkaloid of Ergot, Nature **137**: 111, 1936; Pharmaceut. J. **136**: 182 (Jan. 25) 1936; New Alkaloids of Ergot: Ergosine and Ergosinine, Nature **137**: 1075 (June 27) 1936; footnote 63.

66. Stoll, Arthur, and Burekhardt, Ernst: Ergocristin and Ergocristinine, ein neues Alkaloidpaar aus Mutterkorn, Ztschr. f. physiol. Chem. **250**: 1-6, 1937.

(According to Smith and Timmis<sup>63</sup> the ergoclavine of Kussner is a complex of ergosine and ergosinine.) Ergometrine, like one member in each of the foregoing pairs, is relatively inactive pharmacologically.<sup>64</sup>

A further step in the chemistry of ergonovine is reported by Stoll<sup>65</sup> in that he and Hofmann have synthesized ergobasini (ergometrine) from the pharmacologically inactive components lysergic acid and 2-aminopropanol-1 and in turn have converted the former into the pharmacologically active ergobasin (ergonovine).

#### PHARMACOLOGY

**Toxicity.**—Ergonovine appears to be from three to four times less toxic in mice, rats and rabbits than ergotamine<sup>66</sup> and ergotoxine.<sup>67</sup> On comparison with ergotamine it is ten times less toxic in the cock, intramuscularly, but of approximately equal toxicity in the cat subcutaneously.<sup>68</sup>

The manifestations produced by poisonous doses resemble those caused by the other alkaloids of ergot and are apparently due in no small part to the lysergic acid component of the molecule, as judged by the toxicity results with ergine, a simple amide of lysergic acid.<sup>69</sup> The most common signs of poisoning in the intact animal, which are essentially due to central action, are excitement, tremors, rapid respiration, weakness of the legs and general weakness, pyrexia, vomiting (in the cat on subcutaneous but not on intravenous injection<sup>67</sup>), convulsions and certain signs of sympathetic stimulation—mydriasis, exophthalmos, retraction of nictitating membrane, erection of the hair, vasoconstriction (ears pale and cold in the rabbit) and tachycardia. As a result of experiments on cats involving adrenalectomies and sympathectomies, Brown and Dale<sup>67</sup> conclude that such signs of sympathetic stimulation are a result to only a minor degree of peripheral action and are chiefly due to central stimulation. In rats the metabolic rate is increased by toxic doses of ergonovine.<sup>48</sup>

In fowl, toxic manifestations on intramuscular injection are also very similar to those produced by ergotoxine but probably less severe (incoordination, depression, dyspnea, staggering gait, drooping wings, salivation, diarrhea and comb changes<sup>67</sup>). The same typical picture, beginning in about five minutes, is produced by ergonovine when administered by mouth, whereas ergotoxine only after forty-five to sixty minutes usually produces a slight effect in comparison with that produced by injection.<sup>67</sup> Although ergonovine produces the characteristic cyanosis of the cock's comb<sup>70</sup> (and rat's tail<sup>71</sup>) there is general agreement

that it is much less liable to produce gangrene than is ergotamine and ergotoxine. Also the cyanosis appears somewhat sooner than with ergotoxine and persists for a much shorter time.<sup>67</sup>

**Circulatory Effects.**—Ergonovine injected intravenously into anesthetized rabbits and spinal cats causes a rise in blood pressure which, in the former animal, is more marked than that resulting from ergotoxine and ergotamine but less so in the latter.<sup>72</sup> In cats anesthetized with chlorbutanol the usual but not invariable effect is a feeble pressor response.<sup>73</sup> In vagotomized dogs under artificial respiration and chloralose anesthesia a strong pressor effect with renal vasoconstriction results.<sup>74</sup> Under evipal, a slight rise in blood pressure with a marked fall in kidney volume occurs.<sup>75</sup> Repeated doses result in a lessened pressor response or hypotension, as is characteristic with other ergot alkaloids.<sup>76</sup> In human subjects ergonovine produces practically no effects<sup>15</sup> or causes a slight increase in systolic and diastolic blood pressure with a slight slowing of the pulse, the effect being about half as great as that produced by ergotamine tartrate.<sup>77</sup>

In contrast, a fall in blood pressure is produced by ergonovine in anesthetized (ether, chloralose, evipal) cats<sup>78</sup> and etherized dogs.<sup>48</sup> Brown and Dale<sup>67</sup> believe that this depressor effect, which is accentuated by depressed respiration, is due to a depression of some vasomotor controlling center in the forebrain, the pressor effect being chiefly due to an action on spinal vasomotor centers rather than to peripheral effects. "The vasomotor effects of the alkaloid are the resultants of a complicated antagonism of actions at different levels."<sup>67</sup>

In contrast to the vasodilatation produced on perfusion of the hind limbs of the cat,<sup>67</sup> the leg vessels of the frog<sup>48</sup> and the ear vessels of the rabbit<sup>68</sup> are constricted by ergonovine.

The action on the heart itself appears to be unimportant in the production of the circulatory effects. Although decrease in the rate and amplitude of the frog heart on perfusion with ergonovine  $1:10^4$  has been observed,<sup>48</sup> negative results have been reported from experiments on the isolated cat<sup>66</sup> and rabbit<sup>67</sup> heart.

In the rabbit, ergonovine inhibits the effect of stimulation of the depressor nerve but is only about one-half as strong in this regard as ergotamine.<sup>74</sup>

**Uterine Action.**—The high sensitivity of the human uterus to ergonovine emphasized in earlier reports<sup>79</sup> is in agreement with the results of animal experimentation in which uterine stimulation is the only specific effect produced by small doses of the alkaloid.

Ergonovine in very high dilutions ( $1:2 \times 10^6$ ,  $1:3 \times 10^6$ ,  $1:5 \times 10^6$ ,<sup>1</sup>) stimulates the isolated rabbit uterus to prompt and prolonged rhythmic contrac-

63. Smith, Sydney, and Timmis, Geoffrey Millward: The Alkaloids of Ergot: Part VIII. New Alkaloids of Ergot: Ergosine and Ergosinine, *J. Chem. Soc.*, 1937, p. 396.

64. The Relationship of the Recently Discovered Ergot Alkaloids, *Brit. M. J.* 2:1114 (Dec. 7) 1935. Chen, K. K.; Swanson, E. E., and Hargreaves, C. C.: Ergometrine, *Proc. Soc. Exper. Biol. & Med.* 34:183-185 (March) 1936. Raymond-Hamet: L'action physiologique de l'ergometrine, est-elle supérieure, égale ou inférieure à celle de son isomère l'ergotamine? *Compt. rend. Soc. de biol.* 120:1208-1212 (Dec. 21) 1935. Stoll, Rothlin, Löffler and Dale.<sup>10</sup>

65. Stoll, Arthur: Active Constituents of Ergot, *Pharm. Monatsschr.* 18:146, 1937; footnotes 41 and 60.

66. Rothlin (footnotes 68 and 71).

67. Brown, G. L., and Dale, Sir Henry: The Pharmacology of Ergometrine, *Proc. Roy. Soc., London s. B* 118:446-477 (Oct. 3) 1935.

68. Rothlin, E.: Ueber ein neues Mutterkornalkaloid, *Schweiz. med. Wehnschr.* 65:947 (Sept. 28) 1935.

69. Brown and Dale.<sup>67</sup> Rothlin.<sup>2</sup>

70. Custer, R. P.: The Experimental Pathology of Ergotism, *Am. J. M. Sc.* 195:452-457 (April) 1938. Rothlin.<sup>71</sup> Brown and Dale.<sup>67</sup> Davis, Adair, Chen and Swanson.<sup>48</sup> Thompson.<sup>7</sup>

71. Rothlin, E.: Sur les propriétés pharmacologiques d'un nouvel alcaloïde de l'ergot de seigle, l'ergobasine, *Compt. rend. Soc. de biol.* 119:1302-1304 (July 20) 1935.

72. Brown and Dale.<sup>67</sup> Davis, Adair, Chen and Swanson.<sup>48</sup> Rothlin, footnotes 68 and 71.

73. Thompson, footnotes 7 and 75.

74. Raymond-Hamet: Sur quelques effets pharmacologiques de l'ergometrine, nouvel alcaloïde de l'ergot de seigle, *Compt. rend. Acad. d. sc.* 201:176-179 (July 8) 1935.

75. Thompson, Marvin, R.: A Comparison of the Pharmacological Syndromes of Ergotetrate (Ergonovine) and the Ergotoxine Group of Ergot Alkaloids, *J. Am. Pharm. A.* 26:805-816 (Sept.) 1937.

76. Brown and Dale.<sup>67</sup> Raymond-Hamet.<sup>74</sup>

77. Lennox, William G., and Leonhardt, Hildegard C.: The Flow and Concentration of Blood as Influenced by Ergot Alkaloids and as Influencing Migraine, *Ann. Int. Med.* 11:663-670 (Oct.) 1937. Lennox, W. G.: Ergonovine versus Ergotamine as a Terminator of Migraine Headache, *Am. J. M. Sc.* 195:458-468 (April) 1938.

78. Rothlin.<sup>71</sup> Davis, Adair, Chen and Swanson.<sup>48</sup> Brown and Dale.<sup>67</sup> Thompson.<sup>75</sup>

79. Davis, Adair, Rogers, Kharasch and Legault,<sup>9</sup> Dudley and Mcir,<sup>14</sup> Kharasch and Legault.<sup>14</sup>

tions<sup>60</sup> in contrast to the relative lack of sensitivity to ergotoxine.<sup>61</sup> Rothlin records the effect on the rabbit uterus in vitro<sup>68</sup> and in situ<sup>82</sup> as being twice as strong as that of ergotamine corresponding to their molecular weights and states that it is more easily washed out in vitro than ergotamine.<sup>82</sup> A much greater difference between the effective doses of these two alkaloids on the puerperal rabbit uterus in situ is indicated by other work.<sup>83</sup>

The isolated uterus of the virgin guinea pig is even more sensitive,<sup>81</sup> responding to dilutions of 1:10<sup>7</sup>,<sup>85</sup> 1:2 × 10<sup>7</sup>,<sup>48</sup> or even to 1:10<sup>9</sup>.<sup>67</sup> However, this preparation shows equal sensitivity to ergotoxine, although the response to the former drug is slightly more abrupt.<sup>67</sup> In the guinea pig as in other animals the most striking effects are on the uterus in situ, within a few days after parturition, the response to intravenous injection being more prompt than with ergotoxine and stimulation of rhythm being the outstanding effect, whereas increases in tone predominate with the latter drug.<sup>67</sup>

Ergonovine increases the tone and activity of the nonpregnant cat uterus, virgin or parous, but in a manner indistinguishable from ergotoxine and ergotamine, as is also true in the early stages of pregnancy. However, the puerperal uterus shows striking sensitivity, ergonovine 1:75 × 10<sup>6</sup> initiating contractions continuing for hours in otherwise quiescent isolated preparations.<sup>67</sup> The uterus in situ behaves similarly,<sup>67</sup> responding to doses of from 0.05 to 0.1 mg. intramuscularly, while ergotamine usually produced no activity in doses up to 2 mg.<sup>83</sup>

A high degree of sensitivity has also been reported for the puerperal dog uterus in situ.<sup>86</sup>

Abortion has been produced in animals by ergonovine, but the results are too variable and few in number to justify a definite statement regarding the necessary dosage and probability of occurrence.<sup>87</sup>

Apparently the outstanding features of the action of ergonovine on animal uteri are manifested in the puerperal period when its prompt action and its effectiveness in small doses or high dilutions distinguish it from ergotoxine and ergotamine. The uterus in situ responds essentially by increased rhythmic contractions,<sup>88</sup> continuing for hours,<sup>80</sup> although an increase in tone is a prominent effect in the initial stages of the action.<sup>90</sup>

**Sympathomimetic Action.**—Ergonovine produces mydriasis on local application,<sup>48</sup> and mydriasis and exophthalmos in the general action of toxic doses in rabbits and cats in contrast to ergotoxine<sup>67</sup> and ergot-

amine,<sup>91</sup> the usual effect of which in the cat is myosis. A relaxation of the isolated intestine of the rabbit is produced, which may be prevented by ergotoxine<sup>48</sup> or ergotamine.<sup>10</sup> In contrast, the guinea pig's jejunum responds by a tonic contracture, which may also be annulled by ergotoxine,<sup>67</sup> and Thompson<sup>75</sup> reports relaxation followed by contraction of the isolated intestine of the guinea pig. Even the response of the isolated uterus of the rabbit is diminished by ergotoxine,<sup>92</sup> just as the latter drug abolishes the effect of epinephrine on this tissue. The blood sugar of the rabbit and dog is increased very little by ergonovine, but it increases the action of epinephrine in this regard.<sup>93</sup> Such observations indicate a peripheral sympathomimetic action, although, as already mentioned,<sup>67</sup> the manifestations of sympathetic stimulation in the intact animal may be due principally to a central effect.

**Epinephrine Inhibiting Action.**—Neither the general pressor response of epinephrine<sup>94</sup> nor its vasoconstricting effect in the kidney and intestine in situ,<sup>66</sup> in the Laewen-Trendelenburg frog perfusion<sup>48</sup> and in the perfusion of the hind limbs of the cat,<sup>67</sup> is prevented by ergonovine as it is by ergotoxine and ergotamine. The same failure of ergonovine to inhibit the action of epinephrine has been demonstrated on the rabbit uterus<sup>95</sup> and the seminal vesicle of the guinea pig.<sup>96</sup> However, it may not be entirely devoid of this action, as it has been observed to some degree on the circulatory system<sup>97</sup> and uterus<sup>98</sup> after very large and repeated doses. Even when such action does appear on in vitro preparations it may be removed by a change in solution, which is not possible with ergotoxine.<sup>67</sup>

**Additional Actions.**—Large doses of ergonovine produce an increase in rate but a decrease in the volume of respiration in cats and rabbits,<sup>66</sup> the respiratory center of the cat being more strongly affected than with ergotamine.<sup>91</sup> Toxic amounts lower the temperature of the mouse<sup>98</sup> and increase that of the cat and rabbit,<sup>99</sup> the latter effect being greater than that with ergotamine.<sup>91</sup> Ergonovine, in doses not producing side actions, produces diuresis in dogs in contrast to the antidiuretic action of ergotoxine and ergotamine.<sup>100</sup> This action is not observed clinically.<sup>15</sup> In vitro it inhibits the splitting of acetylcholine by choline esterase.<sup>101</sup>

**Occurrence and Assay.**—It was recognized early in the investigation of ergonovine that it did not occur in constant amounts in all specimens of ergot, and in certain samples (e.g. Russian ergot in contrast to Spanish and Portuguese ergots) it was entirely lacking.<sup>102</sup> Even ergots obtained from one locality may vary in this regard.<sup>103</sup> The results of various workers indicate a content of from 0.05 to 0.2 mg. per gram

80. Rothlin.<sup>71</sup> Brown and Dale.<sup>67</sup> Davis, Adair, Chen and Swanson.<sup>48</sup> Thompson.<sup>7</sup>

81. Thompson.<sup>7</sup> Davis, Adair, Chen and Swanson.<sup>48</sup> Brown and Dale.<sup>67</sup> 82. Rothlin, E.: Neues zum Mutterkornproblem, Arch. f. exper. Path. u. Pharmacol. **181**: 154-155, 1936.

83. Oettel, H., and Bachmann, H.: Säugetieruterus über Hypophysin, Ergon Arch. f. exper. Path. u. Pharmacol. **181**: 154-155, 1936.

84. Thompson.<sup>7</sup> Davis, Adair, Chen and Swanson.<sup>48</sup> Brown and Dale.<sup>67</sup> Küssner and Sieckmann.<sup>85</sup> Thompson.<sup>75</sup>

85. Küssner, W., and Sieckmann, W.: Ergometrin, ein neues Mutterkornalkaloid, München. med. Wehnschr. **83**: 725-726 (May 1) 1936.

86. Davis, Adair, Chen and Swanson.<sup>48</sup> Swanson, Hargreaves and Chen.<sup>107</sup> Azuma, Kumagai and Usui.<sup>88</sup> Küssner and Sieckmann.<sup>85</sup>

87. Reisel, J. H.: Ergot Preparations, Acta brev. Neerland. **7**: 81-82, 1937; Chem. Abstr. **31**: 6329, 1937. Thompson.<sup>4</sup> Brown and Dale.<sup>67</sup> Rothlin.<sup>68</sup>

88. Azuma, A.; Kumagai, H., and Usui, T.: Effect of New Alkaloid Ergonovine (Ergonovine) on Chronic Uterine Fistula in Unanesthetized Dog, Jap. J. M. Sc. IV, Pharmacol. **9**: 205-206, 1936. Brown and Dale.<sup>67</sup> Küssner and Sieckmann.<sup>85</sup>

89. Brown and Dale.<sup>67</sup> Küssner and Sieckmann.<sup>85</sup> 90. Oettel and Bachmann.<sup>83</sup> Davis, Adair, Chen and Swanson.<sup>48</sup>

91. Rothlin, footnotes 68 and 82. 92. Swanson, Hargreaves and Chen.<sup>107</sup> Thompson, footnotes 7 and 75.

93. Rothlin, E.: Pharmacologische Grundlagen der Mutterkorntherapie, München. med. Wehnschr. **84**: 321-322 (Feb. 26) 1937; footnotes 68 and 71.

94. Rothlin, footnotes 68 and 71. Davis, Adair, Chen and Swanson.<sup>48</sup> Brown and Dale.<sup>67</sup> Thompson, footnotes 7, 26 and 75. Raymond-Hamet.<sup>74</sup>

95. Rothlin, footnotes 68 and 71. Davis, Adair, Chen and Swanson.<sup>48</sup> Küssner and Sieckmann.<sup>85</sup> Chen, Swanson, Kleiderer and Clowes.<sup>25</sup>

96. Brown and Dale.<sup>67</sup> Rothlin.<sup>68</sup> 97. Davis, Adair, Chen and Swanson.<sup>48</sup> Brown and Dale.<sup>67</sup> Raymond-Hamet.<sup>74</sup> Rothlin.<sup>68</sup>

98. Thompson, footnotes 7 and 75. Brown and Dale.<sup>67</sup> 99. Rothlin, footnotes 68 and 82. Brown and Dale.<sup>67</sup>

100. Zunz, Edgar, and Vesselovsky, Olga: Action de l'ergometrine et de l'ergobasine sur la diurese, Compt. rend. Soc. de biol. **120**: 1360-1362 (Nov. 20) 1935; **126**: 270-272 (No. 25) 1937.

101. Navratil, Ernst: Ueber die Beeinflussung der Cholinesterase durch Ergobasine, Klin. Wehnschr. **16**: 64-65 (Jan. 9) 1937.

102. Kharasch and Legault.<sup>11</sup> Stoll, Rothlin, Löffler and Dale.<sup>30</sup> Stoll.<sup>41</sup> 103. A. M. A. **109**: 1631-1635 (Nov. 13) 1937.

of ergot in samples which contain it.<sup>104</sup> Of course, a part of this variation may be due to the efficiency of isolation and to the purity of the final product. In any case it is present in much smaller concentrations than the ergotoxine-ergotamine group, which may reach 2 mg. per gram<sup>105</sup> and according to U. S. P. requirements must be 0.5 mg. per gram.

Owing to such variations in occurrence and to the marked activity of ergonovine on the uterus in comparison with that of other ergot alkaloids, the problem of assay is of great importance and has been considered in numerous publications.<sup>106</sup> The assay of pure preparations of ergonovine uncontaminated by other alkaloids of ergot is a comparatively simple problem, a variety of tests being applicable.<sup>107</sup> However, in crude preparations containing such other alkaloids as ergotoxine and ergotamine it becomes more difficult, since the latter produce comparable results in the colorimetric and cock's comb methods. Consequently such assays would be a measure neither of the content of any particular alkaloid nor of the clinical potency of the preparation. Although ergonovine has a much stronger effect than the other alkaloids on the isolated rabbit uterus, even by this method the presence of the latter substances and also of amines in galenic preparations would be complicating factors. This is especially true, if, as already stated, the response of the isolated rabbit uterus to ergonovine is diminished by ergotoxine.<sup>108</sup> It would appear that a separation of ergonovine from the other group of alkaloids would be necessary before assay, unless such assays were made clinically on the postpartum human uterus. Assays by the colorimetric method<sup>109</sup> and on the puerperal cat or rabbit uterus *in situ*<sup>83</sup> involving a previous separation have already been proposed. Naturally the usefulness of such methods must be learned by further experience with them. Of course, a simpler solution of the problem from the therapeutic point of view would be the use of pure alkaloids rather than of galenic preparations. Such a practice would also be desirable with regard to the production of the specific effects of the individual alkaloids.<sup>10</sup>

#### CLINICAL INVESTIGATIONS

*Effective Dosages and Character of Action.*—It was early observed that the postpartum uterus is extremely sensitive to ergonovine. Effective dosages originally cited by Dudley and Moir<sup>16</sup> were from 0.5 to 1 mg. orally, from 0.25 to 0.5 mg. intramuscularly and from 0.05 to 0.1 mg. intravenously. Positive effects have been produced with less than 0.05 mg. intravenously, although 0.2 mg. has been described as an optimal intravenous dose and 0.4 mg. is considered suitable for administration by mouth, sublingually or intramuscularly.<sup>15</sup> Typical responses may be obtained, however, from 0.2 mg. by mouth.<sup>21</sup> Doses of approximately this range have proved effective in other investigations<sup>110</sup>

and have been safely increased to 1.5 mg. by mouth and 0.75 mg. intramuscularly.<sup>111</sup>

The rapidity of response has proved to be a distinctive feature in contrast to the prolonged latent period characteristic of the other alkaloids. The time elapsing between administration and effect is approximately from six to eight minutes, from three to four minutes and from one to two minutes or less after administration by mouth, intramuscularly and intravenously respectively. On the contrary, ergotoxine and ergotamine, in doses by mouth as high as 3 mg. or more, which produce unpleasant side effects, may cause no action on the uterus or the action may appear only after a latent period of from one half to three quarters of an hour or longer.<sup>112</sup> Even on injection, twenty minutes may elapse before the onset of action.<sup>111</sup>

The character of the response has also been described in detail in these studies. On the quiescent postpartum uterus an intravenous injection results in an abrupt increase in tone developing over the course of about fifteen seconds. This is followed by slight and increasing contractions with some fall toward normal in tone, the record henceforth resembling that following administration by other routes.<sup>15</sup> In the latter cases the development in tone is less rapid, with slight contractions which gradually become less frequent. The early phase of the action, lasting for from forty-five to ninety minutes, has been described as a tonicoclonic stage in which a tonic contraction is the predominant feature.<sup>113</sup> The early spasm is considered to be due to contractions following each other in such close succession that the uterus does not have time to relax.<sup>50</sup> With a gradual decrease in tone accompanied by a greater prominence of rhythmic contractions this phase gradually changes into one lasting up to three hours or longer characterized by successive rhythmic contractions with complete relaxation intervening, the contractions becoming less frequent and weaker as the effect subsides. The tonic element of the action is apparently less marked than that resulting from ergotoxine and ergotamine,<sup>111</sup> the tonus increase being proportionately small in relation to the rhythmic contractions produced.<sup>114</sup>

*Duration of Action.*—The early assumption<sup>115</sup> that the action of ergonovine on the uterus is abrupt and transient in comparison with a more persistent effect produced by ergotoxine and ergotamine might well have been inferred, owing to its high water solubility and consequent easier removal from its site of action, as indeed has been observed in *in vitro* experiments.<sup>82</sup> However, in both animal<sup>80</sup> and clinical<sup>116</sup> investigations it has been demonstrated that the action persists for from three to four hours or longer. Rothlin,<sup>117</sup> Stoll,<sup>60</sup> Heyrowsky<sup>118</sup> and Wirth<sup>119</sup> consider this duration of action to be overestimated on account of the possible contamination with ergotoxine and ergotamine

104. Dudley and Moir.<sup>16</sup> Dudley.<sup>17</sup> Stoll and Burekhardt.<sup>15</sup> Stoll.<sup>11</sup> Rothlin.<sup>100</sup> Thompson.<sup>7</sup>

105. Rothlin, E.: Ueber die Standardisierung von Mutterkorn, Arch. f. Exper. Path. u. Pharmacol. **184**: 69, 1936.

106. Thompson.<sup>7</sup> Swanson, Hargreaves and Chen.<sup>107</sup> Hampshire and Page.<sup>126</sup> Rothlin.<sup>108</sup> Oettel and Bachmann.<sup>83</sup>

107. Swanson, Edward E.; Hargreaves, Chester C., and Chen, K. K.: The Question of Assaying Ergotocine, the New Ergot Principle, J. Am. Pharm. A. **24**: 835-839, 1935.

108. Thompson, footnotes 7 and 75. Swanson, Hargreaves and Chen.<sup>107</sup>

109. Trabuechi, Emilio: The Determination of Ergonovine in Ergot Preparations, Boll. Soc. ital. biol. sper. **12**: 232-234 (June) 1937. Glycart, C. K.: Report on the Chemical Assay for Ergot Alkaloids, J. A. Official Agric. Chemists **20**: 566-568, 1937. Hampshire and Page.<sup>126</sup>

110. Kharasch and Legault.<sup>11</sup> Davis.<sup>100</sup> Hauck and Möller-Christensen.<sup>113</sup> Moir, footnotes 50 and 111.

111. Moir, Chassar: The Merits and Demerits of Oxytocic Drugs in the Postpartum Period, Proc. Roy. Soc. Med. **28**: 1654 (2) 1935; Use of Oxytocic Drugs Postpartum, Brit. M. J. **2**: 178-179 (July 27) 1935.

112. Adair, Davis, Kharasch and Legault.<sup>12</sup> Moir.<sup>111</sup>

113. Hauck, E., and Möller-Christensen, E.: Preliminary Results with Ergonovine, Acta obst. et gynec. Scandinav. **16**: 152-159, 1936; New Ergot Preparations—Ergometrine, J. Obst. & Gynec. Brit. Emp. **43**: 1145-1151 (Dec.) 1936.

114. Runge, H.: Ueber Erfahrungen mit Ergometrin, Zentralbl. f. Gynäk. **60**: 1986-1990 (Aug. 22) 1936.

115. Burn, J. H.: The Isolation of Ergometrine, Pharmacol. J. **134**: 357 (March 30) 1935. Stoll, Rothlin, Löffler and Dale.<sup>10</sup>

116. Adair, Davis, Kharasch and Legault.<sup>12</sup> Stoll.<sup>11</sup> Hauck and Möller-Christensen.<sup>113</sup> Moir, footnotes 50 and 111. Antoine.<sup>121</sup>

117. Rothlin, E.: The Present Status of the Ergot Problem, M. Rec. **245**: 449-452 (June 2) 1937; footnote 93.

118. Heyrowsky, K.: Neo-Gynergen, ein Präparat aus reinen Mutterkornalkaloiden, Zentralbl. f. Gynäk. **61**: 42-46 (Jan. 2) 1937.

119. Wirth, L.: Klinische Erfahrungen mit einem neuen Mutterkornwirkstoff, München. med. Wchnschr. **84**: 324 (Feb. 26) 1937.

of the ergonovine preparations used and on account of the previous administration of ergotoxine or ergotamine in certain clinical experiments which might account for the prolonged action observed. However, it is doubtful whether such criticisms could apply in many instances. Although the action may persist as stated, the duration of the spasm may be only half that of the ergotamine-ergotoxine group and the total duration of the effect probably less than that of these alkaloids.<sup>120</sup>

**Side Actions.**—A favorable aspect in the clinical use of ergonovine is the rarity of undesirable side actions, which frequently occur with the other alkaloids,<sup>121</sup> and posterior pituitary extract.<sup>122</sup> In one series of more than 200 cases in which 0.25 or 0.5 mg. of ergonovine was administered orally, no side actions were observed.<sup>114</sup> However, in a few cases nausea and vomiting has been encountered,<sup>15</sup> and Moir<sup>123</sup> reports three instances of unusual reactions.

#### THERAPEUTIC USES

Before the onset of labor the uterus is apparently somewhat insensitive to the action of ergonovine,<sup>50</sup> although some effect has been reported.<sup>121</sup> It gave inconclusive results when it was tried in a few cases for the induction of labor<sup>15</sup> and for the interruption of a four to five months pregnancy.<sup>114</sup> Also in cesarean section the uterus does not respond to ergonovine before removal of the fetus unless labor has already commenced.<sup>50</sup>

Its administration in labor before the birth of the child is considered unsafe<sup>125</sup> although it has been used in a few selected cases of uterine inertia in the second stage of labor with successful results.<sup>114</sup>

Ergonovine probably finds its most extensive application in the treatment of postpartum hemorrhage, having been successfully used in several series of cases.<sup>126</sup> It is probably more reliable for this purpose than posterior pituitary extract.<sup>127</sup>

If necessary it may be safely used in the third stage of labor in doses of approximately 0.25 mg. by injection or by mouth, as indicated by several investigations involving this procedure.<sup>128</sup> The usual but not invariable result has been rapid placental separation and expulsion with minimal bleeding. Moir<sup>111</sup> favors its use in cases of third stage hemorrhage or on failure of simple methods to produce placental expulsion but not as a routine procedure.

The final answer regarding the use of ergonovine in the puerperium has not been reached, although there have been several controlled studies in this regard. Davis, Adair and Pearl<sup>21</sup> and Wirth<sup>119</sup> report favorably concerning its action in reducing foul lochia, lochial obstruction, subinvolution and morbidity. Der Brucke<sup>129</sup> and Tuck<sup>130</sup> (ergoklonin) also consider it

to be of benefit. On the contrary, Moir<sup>121</sup> reached the tentative conclusion that its routine use in the puerperium offered no advantages and considered it contraindicated in the presence of uterine sepsis.

Uniformly satisfactory results are reported for its use in cesarean section with respect to prompt separation of the placenta and the control of hemorrhage. It has been injected as the baby was delivered,<sup>15</sup> before incision of the uterus,<sup>50</sup> and directly into the uterine wall after extraction of the baby.<sup>119</sup>

It would appear that ergonovine is worthy of further trial in the treatment of incomplete abortion.<sup>121</sup> Although not all reports are favorable regarding the expulsion of retained secundines, it is undoubtedly of value in the control of bleeding.

After diagnosis it may be of value as a palliative and temporary measure in certain cases of menorrhagia and metrorrhagia until the underlying pathologic condition can be corrected.<sup>133</sup>

Positive results have been reported for the relief of migraine headache by ergonovine, although it was effective in a much lower percentage of cases than was ergotamine.<sup>77</sup>

**Importance of Ergonovine.**—The isolation and clinical trial of ergonovine has prompted the expression of various opinions regarding its importance in the realm of ergot therapy. Dale<sup>131</sup> and Dudley and Moir<sup>18</sup> consider it of greater therapeutic importance than all the hitherto known alkaloids of ergot and believe that it forms the basis for ergot therapy at least as far as the uterine action is concerned. It is suggested that the presence of the other alkaloids may actually have a deleterious effect. Moir<sup>50</sup> expresses the belief that it should be used wherever there are indications for ergot therapy and that it completely supplants the older preparations.

Adair<sup>15</sup> hails it with similar enthusiasm, considering it the active principle which is responsible for most if not all of the desirable oxytocic effect of ergot. Runge<sup>114</sup> and Küssner<sup>135</sup> also seem to agree that it is of prime importance in ergot therapy. Stoll<sup>136</sup> considers such opinions too sanguine: Owing to the small amounts of ergonovine in many ergots, the traditional action of the crude drug may not be wholly explained by its presence. Also in the light of its presumably short duration of action it plays only a limited role in ergot therapy and should be supplemented by a drug with a more persistent action when this is desired. Furthermore, it has been pointed out by Rothlin and Löffler<sup>10</sup> that it at least cannot replace ergotoxine and ergotamine in the treatment of those conditions in which the inhibiting effect on the sympathetic nervous system is indicated. The wide therapeutic use which already exists will undoubtedly settle such differences of opinion in the near future.<sup>137</sup>

120. Moir, footnotes 50 and 111. Antoine.<sup>121</sup>  
121. Davis, Adair, Rogers, Kharasch and Legault.<sup>9</sup> Dudley and Moir.<sup>10</sup>  
122. Adair, Davis, Kharasch and Legault.<sup>15</sup> Davis.<sup>103</sup> Moir.<sup>111</sup>  
123. Moir, Chassar: *Ergometrine: The Possibility of Idiosyncrasy*, Brit. M. J. 2: 1028 (Nov. 21) 1936.  
124. Antoine, Tassilo: Die klinische Verwendbarkeit der neuen Secale-Alkaloides Ergobasin, Wien. klin. Wchnschr. 50: 999-1001 (July 2) 1937.  
125. Moir.<sup>50</sup> Runge.<sup>114</sup>  
126. Moir.<sup>50</sup> Adair, Davis, Kharasch and Legault.<sup>15</sup> Davis, Adair and Pearl.<sup>21</sup> Hauck and Möller-Christensen.<sup>113</sup> Wirth.<sup>119</sup> Runge.<sup>114</sup>  
127. Moir.<sup>50</sup> Adair, Davis, Kharasch and Legault.<sup>15</sup> Wirth.<sup>119</sup>  
128. Tritsch, J. E., and Behm, K. H.: Clinical Experience with a New Ergot Alkaloid, Am. J. Obst. & Gynec. 34: 676-679 (Oct.) 1937. Adair, Davis, Kharasch and Legault.<sup>15</sup> Moir.<sup>111</sup> Runge.<sup>114</sup> Tuck.<sup>130</sup>  
129. Der Brucke, M. G.: Notes on the Use of the Recently Introduced Ergot Alkaloids in the Puerperium, Am. J. Obst. & Gynec. 32: 474-478 (Sept.) 1936.  
130. Tuck, Vernon L.: A Clinical Test of the Newly Recognized Oxytocic Principle of Ergot and a New Method of Administration, Am. J. Obst. & Gynec. 30: 718-723 (Nov.) 1935.

131. Moir, footnotes 50 and 111.  
132. Davis, Adair and Pearl.<sup>21</sup> Moir.<sup>50</sup> Runge.<sup>114</sup> Wirth.<sup>119</sup>  
133. Davis, Adair and Pearl.<sup>21</sup> Davis.<sup>103</sup> Moir.<sup>50</sup> Runge.<sup>114</sup>  
134. Dale, Sir Henry: Die Pharmakologie des Mutterkorns, Schweiz. med. Wchnschr. 65: 885 (Sept. 14) 1935. Stoll, Rothlin, Löffler and Dale.<sup>10</sup>  
135. Küssner, W.: Recent Results in Ergot Research, Angew. Chem. 50: 34-38, 1937.  
136. Stoll, Rothlin, Löffler and Dale.<sup>10</sup> Stoll, footnotes 41 and 60.  
137. Reviews not directly referred to in the text:  
Barger, George: The Alkaloids of Ergot, Analyst 62: 340-354 (May) 1937.  
Tanret, G.: Recent Discoveries in the Chemistry of Ergot, 1930-1935, J. Pharm. Chim. 24: 269-283, 1936.  
Nelson, Erwin E., and Calvery, Herbert O.: Present Status of the Ergot Question, Physiol. Rev. 18: 297-327 (April) 1938.

## SUMMARY

Ergonovine, an alkaloid of ergot, was isolated independently and by contemporaneous work in four laboratories.

It crystallizes readily and forms a variety of crystalline salts; characteristic physical properties have been described for both the base and the salts.

In contrast to other alkaloids of ergot, ergonovine is appreciably soluble in water and comparatively insoluble in chloroform; its salts are markedly soluble in water.

It is less readily precipitated by Mayer's reagent than other ergot alkaloids but gives the characteristic color reactions of this group. The color developed with *p*-dimethylaminobenzaldehyde is quantitatively greater than with the other alkaloids, in keeping with the smaller molecule of ergonovine.

Ergonovine,  $C_{19}H_{23}O_2N_3$ , consists of a combination of lysergic acid, common to all ergot alkaloids, and *d* 2-amino propanol-1.

In the intact animal and in human subjects the only appreciable effect of moderate doses is on the uterus, which is especially sensitive in the puerperal state. It is effective in smaller doses and concentrations than are other ergot alkaloids, such doses being remarkably free from unpleasant side actions. It is further characterized by its prompt action even when administered by mouth. It increases both the tone and the rate and amplitude of rhythmic contractions of the uterus, the latter effect probably being proportionately greater than the tonus changes. The duration of the effect, although probably less than that of ergotoxine and ergotamine, is at least comparable with that of the latter alkaloids.

It is less toxic than ergotoxine and ergotamine but in poisonous doses produces effects similar to those of the latter alkaloids. Although ergonovine produces the characteristic cock's comb reaction, it shows definitely less tendency to produce gangrene than ergotoxine and ergotamine.

The circulatory effects, which are referable to actions on the central nervous system and peripheral vascular mechanism rather than to cardiac effects, vary with the animal and with experimental conditions.

Ergonovine shows a definite sympathomimetic effect and little or no inhibition of epinephrine action.

It may be assayed by a variety of procedures when in the pure form but at present cannot be quantitatively determined in the presence of other alkaloids of ergot. Suggested methods involve a separation of ergonovine from the ergotoxine-ergotamine group before assay.

Its greatest clinical value appears to be in the treatment of postpartum hemorrhage, being safely administered at the beginning of the third stage if necessary. Likewise it has been of value in the control of hemorrhage following cesarean section. Many investigators favor its use in the puerperal period for the promotion of involution and the prevention and control of sepsis, but this use is not universally accepted. Variant results have also been obtained in the treatment of incomplete and inevitable abortion. It may be used as a palliative measure in certain cases of menorrhagia and metrorrhagia.

Many authorities believe that ergonovine forms the basis for all ergot therapy involving uterine action and that it is responsible for the traditional effect of ergot, while others are less enthusiastic concerning its value.

## Council on Foods

## ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION AND WILL BE LISTED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED.

FRANKLIN C. BING, Secretary.

MRS. PALEY'S BABY FOOD—  
STRAINED APPLES

*Manufacturer.*—Paley-Sachs Food Company, Houston, Texas.

*Description.*—Canned cooked sieved apples, containing a small amount of added dextrose.

*Manufacture.*—Colorado Jonathan apples are thoroughly washed, trimmed, inspected, cooked in air-tight steam pressure cookers for five minutes with added dextrose, sieved, filled into glass jars and heat processed.

*Analysis* (submitted by manufacturer).—Moisture 77.4%, total solids 22.6%, ash 0.3%, fat (ether extract) 0.1%, protein ( $N \times 6.25$ ) 0.2%, reducing sugars as dextrose 15.7%, sucrose 1.7%, crude fiber 0.8%, total carbohydrates other than crude fiber (by difference) 21.2%, calcium (Ca) 0.006%, phosphorus (P) 0.02%, iron (Fe) 0.0008%.

*Calories.*—0.9 per gram; 25.6 per ounce.

## CLAPP'S PUREE OF GREEN BEANS

*Manufacturer.*—Harold H. Clapp, Incorporated, Rochester, N. Y.

*Description.*—Canned sieved green beans, seasoned with salt.

*Manufacture.*—Fresh green beans, grown under contract with the manufacturer, are cleaned, sorted, washed, again sorted, and precooked under pressure in an atmosphere of steam. Salt is added and the partially cooked beans are sieved in an atmosphere of steam, vacuum treated to attain the desired consistency, automatically filled into cans, and heat processed.

*Analysis* (submitted by manufacturer).—Moisture 91.5%, total solids 8.5%, ash 0.8%, fat (ether extract) 0.2%, protein ( $N \times 6.25$ ) 1.6%, crude fiber 0.9%, carbohydrates other than crude fiber (by difference) 5.0%.

*Calories.*—0.3 per gram; 8 per ounce.

## CELLU BRAND ORANGE JUICE

*Distributor.*—Chicago Dietetic Supply House, Inc., Chicago.

*Description.*—Canned California Valencia orange juice.

*Manufacture.*—Manufactured in essentially the same manner as Treesweet Pure California Orange Juice (THE JOURNAL, June 15, 1935, p. 2187).

*Analysis* (submitted by manufacturer).—Moisture 85.9%, total solids 14.1%, ash 0.4%, fat (ether extract) 0.1%, protein ( $N \times 6.25$ ) 1.1%, reducing sugar as invert 5.6%, sucrose (by copper reduction) 4.8%, crude fiber 0.02%, carbohydrates other than crude fiber (by difference) 11.5%, titratable acidity as citric acid 1.0.

*Calories.*—0.51 per gram; 14 per ounce.

MRS. PALEY'S BABY FOOD—STRAINED  
EVAPORATED PEARS

*Manufacturer.*—Paley-Sachs Food Company, Houston, Texas.

*Description.*—Cooked, sieved, sulfured dried pears, packed with added dextrose.

*Manufacture.*—Dried sulfured pears are washed, soaked, pressure cooked with added dextrose, strained, filled into glass jars, vacuum sealed and heat processed. A small amount of lemon juice is added for flavor.

*Analysis* (submitted by manufacturer).—Moisture 72.4%, total solids 27.6%, ash 0.5%, fat (ether extract) 0.1%, protein ( $N \times 6.25$ ) 0.6%, crude fiber, 1.4%, reducing sugars as dextrose 13.2%, sucrose 2.2%, total carbohydrate other than crude fiber (by difference) 25.0%, iron (Fe) 0.0011%, phosphorus (P) 0.025%, calcium (Ca) 0.021%, sulfur dioxide (SO<sub>2</sub>) 0.033%.

*Calories.*—1 per gram; 28.4 per ounce.



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SATURDAY, DECEMBER 10, 1938

## GAS GANGRENE

All recent reports on gas gangrene in man agree essentially on the increase of this condition in civil life. Following injuries sustained in the World War gas gangrene was common. Today the condition is becoming more important because of the more frequent occurrence of crushing wounds and lacerations following traffic and industrial accidents. While its frequency is difficult to determine accurately, the increasing reports in the literature seem to offer sufficient evidence of its widespread nature.

A recent review<sup>1</sup> of the morbidity and mortality due to gas gangrene in New York State exclusive of New York City, while admittedly incomplete, reports 208 hospitalized cases between 1932 and 1936. These cases are placed in four groups: those presenting records positive for gas gangrene clinically and bacteriologically, those presenting records incomplete but with sufficient evidence to be included as gas gangrene, those presenting records that made the diagnosis questionable and those in which the data were too incomplete for an accurate diagnosis. With the omission of the last two groups 135 cases were recorded, ninety-one of them resulting from trauma, thirteen from clean amputations, seven from pregnancy, five from gunshot wounds and nineteen from miscellaneous causes. When compared with the incidence of tetanus, infection by this group of spore-bearing bacteria is probably as frequent. According to White,<sup>2</sup> gas infection usually occurs in four types of wounds: crushing injuries in which the skin is torn, puncture wounds with a great deal of hemorrhage, particularly if a foreign body has been implanted, extensive lacerations of tissues with gross soiling with dirt, and badly soiled compound fractures. Ramsay<sup>3</sup> states that gunshot wounds and compound

fractures offer the most favorable environmental conditions for the development of *Clostridium welchii* or other spore-bearing anaerobes, since damaged muscle tissue is the perfect medium for the growth and development of these organisms. Less commonly, gas gangrene has been reported following abortion<sup>4</sup> and as a result of hypodermic injection.<sup>5</sup> Organisms of this group, including *Clostridium welchii*, *Vibrio septique* and *Clostridium oedematiens*, are so widely distributed in nature that little can be done to eradicate the source of infection.

The best treatment for gas gangrene is prophylactic. Penfold and Tollhurst<sup>6</sup> have reported promising attempts at the immunization of animals and man with alum-precipitated formol toxoid made from *Clostridium welchii* toxin. After preliminary work on experimental animals volunteers were treated with the toxoid and the level of antitoxin was measured at various intervals thereafter. The evidence presented, they believe, suggests that this toxoid is suitable material for immunizing man against gas gangrene due to *Clostridium welchii*, although the level of antitoxin necessary for protection has not as yet been determined. Auspicious as this work may be, it is not likely that the frequency of gas gangrene in peace time is such that mass immunization is likely to be a practical preventive measure in the near future.

The prophylactic treatment of patients who have extensive lacerations or other injuries which are recognized as predisposing to gas gangrene has been carefully outlined in a number of the recent discussions. Lower and Tormey<sup>7</sup> state that in carrying out a débridement properly it is important that adequate exposure of the depths of the wound be obtained. The wounds in which dead spaces or pockets are apt to occur are best cared for by placing Dakin tubes in their depths through which irrigation may be carried out every two hours. They also recommend the use of a prophylactic dose of polyvalent gas bacillus antitoxin (and tetanus antitoxin) to every patient with extensive or suspicious wounds. Although Malone<sup>8</sup> believes that a larger dose of *Clostridium welchii* antitoxin is to be preferred to the polyvalent antitoxin usually supplied, the majority seem to agree that the polyvalent antitoxin in suitable quantities is satisfactory.

In spite of suitable precautionary measures there are some instances in which gas gangrene develops, and treatment therefore becomes of paramount importance. Surgical exploration with the introduction of air and probably diluted solution of sodium hypochlorite should

4. Dawbarn, R. Y., and Williams, Bryan: Three Cases of *Cl. Welchii* Infection Following Abortion, *Brit. M. J.* 2: 279 (Aug. 6) 1938.

5. Jungmichel, G.; Kirschner, M., and Haas, H.: Ueber die Gasbrandinfektion nach Injektion, *München. med. Wchnschr.* 85: 125 (Jan. 28) 1938. Bittroff, R.: Ueber Gasbrandinfektion nach Injektion, *ibid.* 85: 590 (April 22) 1938.

6. Penfold, W. J., and Tollhurst, Jean C.: Formol-Toxoids in the Prophylaxis of Gas Gangrene, *M. J. Australia* 1: 982 (June 26) 1937; Prophylaxis of Gas Gangrene in Man, *ibid.* 1: 604 (April 2) 1938.

7. Lower, W. E., and Tormey, T. W., Jr.: Gas Gangrene and Its Treatment, *S. Clin. North America* 17: 1385 (Oct.) 1937.

8. Malone, Battle: Gas Gangrene—Its Prevention and Treatment, *J. Tennessee State M. A.* 30: 402 (Oct.) 1937.

1. Mitchell, O. W. H.; Bryant, T. L., and Chapman, O. D.: Gas Gangrene: Morbidity and Mortality in New York State (Exclusive of New York City)—Based on General Hospital Reports for the Years 1932-1936 Inclusive, *New York State J. Med.* 38: 1022 (July 15) 1938.

2. White, R. J.: Gas Gangrene, *Texas State J. Med.* 34: 271 (Aug.) 1938.

3. Ramsay, C. H.: Gas Gangrene Infections in Industrial Practice with Especial Reference to Infections Following Compound Fractures and Other Accidents, *South. M. J.* 31: 775 (July) 1938.

in this event be employed at once. The use of antitoxin in large quantities intramuscularly or intravenously or in some cases around the infected area is also a procedure to be employed promptly.

The use of x-rays has been reported favorably,<sup>9</sup> and in the past few months several reports on the favorable effect of sulfanilamide or its derivatives in gas gangrene have appeared.<sup>10</sup> The effectiveness of prophylactic measures and improvement and addition of therapeutic techniques for dealing with this disease should do much to minimize its dangers.

#### ANTIGENIC STRUCTURE OF SPERMATOZOA

The recent demonstration of a head-specific and a tail-specific antigenic fraction in mammalian spermatozoa, with a third or species-specific antigen common to the heads and the tails, is of basic biologic and immunochemical interest. Separation of spermatozoa into head and tail fractions was attempted forty years ago by Miescher.<sup>1</sup> He found that if fish spermatozoa are suspended in distilled water the relatively heavy heads can be broken off by carefully graduated centrifugation. Mammalian spermatozoa, however, cannot be broken up by this technic. Henle and his colleagues<sup>2</sup> of the Johnson Foundation for Medical Physics, University of Pennsylvania, have recently attempted such fragmentation by the modern technic of supersonic vibration. They found that bull, dog or rabbit spermatozoa were fairly completely broken up into head and tail fractions by exposure for seven minutes to vibrations of 9,000 cycles per second. Guinea pig spermatozoa required fifteen minutes and human spermatozoa twenty minutes for similar fragmentation. Final separation of the head and tail fragments was effected by fractional centrifugation. By repeated washings, head and tail suspensions can often be obtained 99 per cent pure. This degree of purity was confirmed by the use of a blood counting chamber and by a study of stained smears. Cleavage occurred uniformly at the junction of the midpiece and head except with human spermatozoa. With human cells a small part of the midpiece often remained with the head. No difference was noted in the microscopic appearance of the heads after separation, except with guinea pig spermatozoa, which often lost their acrosoma.

The Pennsylvania investigators immunized rabbits against the head and tail fractions and against the intact spermatozoa of four different animal species. Tests of

antigenic specificity were made by the complement fixation technic with confirmatory tests by slide agglutination. As shown by other investigators, cross reactions were obtained with the intact spermatozoa of different animal species. Cross reactions were obtained also with the head and tail fractions of the same animal species. By proper absorption of the antisera, however, highly specific fractional antibodies were demonstrated. Thermolabile tail-specific and head-specific antigen fractions were thus recognized, as well as a coctostable heterophile or nonspecific fraction common to heads and tails. A fourth, nuclear-specific, fraction is suspected, not demonstrable in intact spermatozoa but readily demonstrable in the broken-off heads. Antibodies against this hypothetical nuclear-specific antigen are not formed on injection of intact spermatozoa but are formed when vibrated heads are injected. Whether or not the suspected nuclear antigen is a protein or a lipid has not yet been determined.

The results obtained by the complement deviation technic were confirmed by a study of slide agglutination. Two types of agglutination were noted. The first was a head-specific agglutination or clumping of the heads, with the formation of a rosette of moving tails. The second was a tail-specific agglutination with adhesion or clumping of the tips of the tails. The latter resulted in a rosette of moving heads. Combined head and tail agglutination was obtained with native antisera against intact spermatozoa, with a resulting netlike entanglement of whole cells.

Immunologists of the future may conceivably regard Henle's work as of basic historical interest, the first successful attempt at a serologic dissection of mammalian tissue cells. There seems no reason why some modification of his technic cannot be applied to other mammalian tissues.

#### NEW JERSEY MOSQUITOES AS POTENTIAL CARRIERS OF YELLOW FEVER

The demonstration by Bennett and his colleagues<sup>1</sup> of the Harvard Medical School that the common New Jersey mosquito is capable of transmitting yellow fever to monkeys seems to throw doubt on the conventional assumptions for other insect-borne diseases. Following experimental proof by Reed, Carroll and their co-workers in 1900-1901 that the subtropical mosquito variously known as *Aedes aegypti*, *Stegomyia fasciata* or *Aedes argentens* is capable of transmitting yellow fever to man, it was quite generally assumed by hygienists that this is the only species of mosquito capable of transmitting this infection. It was alleged in support of this assumption that the geographic distributions of *Aedes aegypti* and yellow fever are the same. Not till a quarter of a century later, after Stokes, Bower and

9. Kelly, J. F., and Dowell, D. A.: Present Status of the X-Rays as an Aid in the Treatment of Gas Gangrene. *J. A. M. A.* **107**: 1114 (Oct. 3) 1936.

10. Bohlman, H. R.: Gas Gangrene Treated with Sulfanilamide: Report of Three Cases. *J. A. M. A.* **109**: 254 (July 24) 1937. Natvig, H.: Eksperimentelle undersøkelser over virkningene av prontosil ved gasspødeminfeksjoner. *Norsk mag. f. laegevidensk.* **99**: 631 (June) 1938. Fuller, G. W., and Kellum, J. M.: Prontosil and Sulfanilamide in the Treatment of Gas Gangrene. *South. Surg.* **7**: 305 (Aug.) 1938.

1. Miescher, Fritz: *Arch. f. exper. Path. u. Pharmacol.* **37**: 100, 1896.

2. Henle, Werner; Henle, Gertrude, and Chambers, L. A.: *J. Exper. Med.* **68**: 335 (Sept.) 1938.

1. Bennett, Byron L.; Baker, Fred C., and Sellards, Andrew Watson: *Science* **88**: 410 (Oct. 28) 1938.

Hudson (1928) had shown that rhesus monkeys are susceptible to yellow fever, was it practicable to make adequate tests of other species. Two other subtropical species of mosquitoes were then shown to be equally efficient vectors of yellow fever, while a third subtropical species would occasionally transmit the disease in an attenuated form.

The question was raised as early as 1904 by J. B. Smith<sup>2</sup> of Trenton, N. J., whether or not the disease could be transmitted by the common northern mosquito. An attempt was not made to answer this question, however, until 1935, when Baker established a colony of *Aedes triseriatus* in his local insectary at Cornell University and sent specimens to the Harvard Medical School for transmission tests. The species bred by Baker is common from Maine to Florida and has been identified as far west as Montana.

At the Harvard Medical School thirty-five of these northern mosquitoes were allowed to feed on a monkey dying from yellow fever. After this feeding the mosquitoes were kept for seventeen days at a temperature of 28 C. (82.4 F.) and six of the seven survivors then allowed to bite a healthy monkey. After an incubation period of six days this monkey showed a transient febrile reaction (104 F.) lasting about twenty-four hours, after which it was without demonstrable symptoms for nearly a month. The monkey, however, died on the thirty-sixth day. Necropsy showed typical appearances of yellow fever.

Bennett and his co-workers have recently repeated this test with four additional monkeys. After being bitten by presumably infected neo-arctic mosquitoes, the four monkeys showed no febrile reaction. Two of them, however, died of yellow fever between the tenth and the thirteenth day. Control intracerebral inoculation of mice with mosquito emulsions showed that 60 per cent of the mosquitoes which had bitten an infected monkey fifteen days previously were carriers of yellow fever. It is nevertheless suggestive that the two monkeys which developed no symptoms had been bitten by mosquitoes kept from fourteen to fifteen days at 28 C., while the two monkeys which died had been bitten by mosquitoes incubated at 37 C. (98.6 F.).

When subtropical mosquitoes are used to infect monkeys with yellow fever there is a usual incubation period of from three to four days, followed by a sharp rise in temperature (104 to 105 F.) lasting from thirty-six to forty-eight hours. This is followed by subnormal temperature and collapse, death almost invariably taking place on the fifth or sixth day. The prolonged incubation period in the Harvard tests, therefore, suggests that the virus of yellow fever is attenuated in the bodies of neo-arctic mosquitoes. Of particular hygienic interest is the evidence that temperature plays an important part

in determining vector infectivity. Somewhat analogous temperature effects have been described for subtropical mosquitoes. This result suggests that low temperature rather than the absence of available insect carriers is the main factor limiting the spread of yellow fever in northern states.

## Current Comment

### TRAFFIC IN OPIUM

With the submission of the report of the Advisory Committee on Traffic in Opium and Other Dangerous Drugs<sup>1</sup> to the Council of the League of Nations, a new and important stage of work in the suppression of the abuse of narcotics appears to have begun. The committee framed a definite statement of the essential principles which might serve as a basis for a future convention on limitation and indicated that this future convention will render possible a final suppression of the use of opium for smoking in countries or territories where the practice is still authorized. Its main purpose will be to develop appropriate measures for a gradual reduction of the quantities of raw opium required for the manufacture of prepared opium. The report of the preparatory committee, which was adopted by the advisory committee, stated as a premise that opium is being produced in quantities far in excess of recognized world requirements. The world requirements of raw opium for purposes recognized in the convention should be ascertained by a system of government estimates similar to that applied under the previous limitation convention. In furnishing such estimates governments would have to state not only the quantities but also the qualities (morphine content) of the opium required. A definite quantitative limit should be fixed annually for the amount of raw opium to be produced by each country. This should be achieved by estimating the requirements and by government agreements not to exceed the estimates in their imports. Estimates of production and requirements should be examined by an international control authority which should have the task of allocating to each producing country on the basis of the estimates the annual quantities to be produced and exported. Furthermore, the convention should consider the methods of regulating stocks of raw opium to be kept in producing and consuming countries and provisions should be made for safeguarding the carrying out of the convention by means of national control. The application of the convention, as in the case of the limitation convention in 1931, should be supervised by an international body entrusted with such powers and duties as shall be specified in the convention. The success of the limitation convention in 1931 has been such as to indicate that this properly international problem of control is now approaching its final phase. While the United States is not a signatory of the League, it has been represented at all the conventions and has ratified all but the 1925 convention for opium control.

2. Smith, J. B.: Report of the New Jersey State Agricultural Experimental Station, Trenton, New Jersey, MacCrellish and Dingley, State Printers, 1904.

1. Report to the Council: Advisory Committee on Traffic in Opium and Other Dangerous Drugs, League of Nations, Geneva, June 24, 1932.

# ORGANIZATION SECTION

## COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

The Council on Medical Education and Hospitals held its usual fall meeting in Chicago on December 4.

### REPORT ON PROGRAM OF FEBRUARY CONFERENCE

A report was made on the program for the next Annual Congress on Medical Education and Licensure to be held in Chicago in February.

### VISITS TO MEDICAL SCHOOLS

Reports of recent visits to medical schools were also considered. The Council noted the progress that had been made toward the preparation of a final report on the survey of medical schools which it is planned to publish in the spring or early summer.

### ACTION ON UNIVERSITY OF ARKANSAS MEDICAL SCHOOL

The University of Arkansas School of Medicine, by vote of the Council, is now listed as being on probation.

### ACTION ON VERMONT AND VIRGINIA COLLEGES

A review of conditions at the University of Vermont College of Medicine and the Medical College of Virginia was postponed until the next academic year.

### APPROVAL OF CERTIFYING BOARD IN ANESTHESIOLOGY

The American Board of Anesthesiology was approved.

### COOPERATION WITH CERTIFYING BOARD IN RADIOLOGY

A plan of cooperation which had been prepared by the Council and the American Board of Radiology was endorsed and it was recommended that other special examining boards be invited to participate in similar plans.

### CONSIDERATION OF HOSPITALS

The usual lists of hospitals desiring registration, intern approval and residency approval were presented and acted on.

### CONFERENCE ON COOK COUNTY HOSPITAL

Representatives of the staff of the Cook County Hospital were informed that, while there has been no change in the status of the Cook County Hospital, the Council appreciates the efforts which have been made to improve conditions and the willingness of the executive committee to cooperate with the Council in further efforts to make it an outstanding center of medical education.

### ACTION ON HOSPITALS APPROVED FOR INTERNSHIP

The Essentials of a Hospital Approved for the Training of Interns were amended so that after Jan. 1, 1940, a minimum of thirty-six necropsies a year will be required, and for a service having 2,000 annual admissions at least three interns will be deemed necessary.

### APPROVED RESIDENCIES

The scope of the Council's list of approved residencies was broadened and its title hereafter will be "Approved Residencies and Fellowships."

The Council voted that at least one year's training in general surgery should be a prerequisite for approved residencies or fellowships in such subdivisions of surgery as urology, orthopedic and thoracic surgery.

### MEETING WITH ADVISORY COMMITTEE

The Council on Medical Education and Hospitals conferred also with a newly appointed advisory committee. Those present included Drs. Ray Lyman Wilbur, J. H. Musser, Fred Moore, Reginald Fitz, Charles Gordon Heyd, Frank H. Lahey, William D. Cutter, Malcolm T. MacEachern, John R. Neal, Charles B. Pinkham, William P. Wherry, Herman G. Weiskotten, Rock Sleyster, Olin West, Morris Fishbein, Oswald N. Andersen, Fritjof H. Arestad, Hamilton H. Anderson and Mr. Homer F. Sanger.

WILLIAM D. CUTTER, M.D., Secretary.

## AMERICAN MEDICAL ASSOCIATION STUDY OF MEDICAL CARE

### Jefferson County, Alabama

The Jefferson County Medical Society report of the Survey of the Need and Supply of Medical Care is so complete in all its phases as to deserve special mention.

Jefferson County occupies an area of 1,124 square miles in the north central portion of Alabama. It has an estimated population of 477,100, of which approximately 38 per cent are Negroes. The city of Birmingham has a population of 289,700, and the two next largest cities, Bessemer and Fairfield, have populations of 21,700 and 13,300 respectively. In addition there are seven other cities and villages with populations varying from 466 to 7,341. Jefferson County is largely dominated by the iron and steel industries.

The county medical society not only conducted the study in an exceptionally thorough manner but also made a careful and scholarly analysis of the facts. The

report of the study and the recommendations filled 131 typewritten pages, which have been permanently bound for future reference. The summary and conclusions which follow are given exactly as they were prepared by the committee in charge of the study.

### SUMMARIZED REPORT OF THE SURVEY

The following report covers the more important details, determined by actual survey, and summarizes the original 140 page report prepared by the secretary of the committee. The procedures used for the collection of data were those outlined by the American Medical Association. The information obtained includes and supplements that requested by the American Medical Association and is intended to furnish the society with all the pertinent facts relative to the problems involved.

The sources of information which form the basis of this study are given in table 1.

The fact that only 58 per cent of all physicians and dentists answered their questionnaires, as compared to 100 per cent of the various agencies, does not necessarily indicate that the professions were the least

TABLE 1.—*Distribution of Questionnaires*

	Number Sent	Number Returned	Per Cent Returned
Physicians and dentists.....	586	342	58.3
Hospitals .....	14	14	100
Nursing organizations .....	3	3	100
Health departments .....	1	1	100
Welfare, relief and unofficial health agencies .....	37	37	100
School systems .....	6	6	100
Colleges .....	3	3	100
Other organizations (chiefly industrial) .....	74	74	100
Pharmacists .....	171	171	100
Totals .....	895	651	72.7

TABLE 2.—*Questionnaires from Physicians and Dentists*

	Number Sent	Per Cent Returned
Physicians, total .....	438	64.4
Members of county medical society.....	352	68.2
Nonmembers of county medical society.....	86	48.8
Dentists .....	148	40.5
Total physicians and dentists.....	586	58.3

interested in the survey. The difference is partially accounted for by the manner in which the data were collected. When agencies did not respond by mail the proper parties were interviewed personally. This procedure was not possible with physicians and dentists. Because of their large number, contact was entirely by mail and by telephone.

Due credit should be given to the various welfare, relief and health agencies for their willingness to furnish all available information; of all the groups approached they appeared to be the most interested and most cooperative.

#### PHYSICIANS AND DENTISTS

There are in Jefferson County 438 physicians and 148 dentists engaged in active practice. This excludes those who have retired and a few who are completely occupied in administrative capacities. There is one physician for each 1,089 of the general population.

The nature of the data requested of members of both professions precludes the presentation of actual figures; only estimates are available, though it is felt (after checking the reports made by physicians with those from the various institutions and agencies) that these estimates are conservative and probably considerably understate the facts.

Returns were received as shown in table 2.

If the data, based on actual reports of 64.4 per cent of all practicing physicians and 40.5 per cent of all practicing dentists, are truly representative of medical and dental practice in this locality, the figures obtained can appropriately be extended to include all those who have not returned their questionnaire. When such figures are combined with data obtained from all the various institutions and agencies, the total charity load may be conservatively estimated as in table 3.

Approximately one half of charity patients applied directly to physicians and dentists and received free treatment, while one half were treated in hospitals and clinics. These figures definitely indicate that the charity

load of physicians in home and office practice is fully as great as the charity load carried by physicians in all institutional practice, including hospitals, outpatient departments and clinics of all the various agencies.

Besides the incalculable number of hours given by physicians in the medical care of hospital inpatients, they devoted an estimate of 41,000 hours to the free care of ambulatory cases in outpatient departments and dispensaries and to preventive medical care in various health centers and clinics. For all this they received nothing except nominal compensation for approximately 5 per cent of their time.

Seventy-four per cent of physicians perform preventive medical services. Of ninety physicians reporting on the amount of preventive medical work done for charity and for pay, 37 per cent stated that they did no charity work, 25 per cent reported that less than 50 per cent of their preventive medical services were for charity, while 38 per cent reported that more than 50 per cent of such work was for charity.

Compensation for preventive medical services (in significant amounts) is made by only two organizations. The health department paid \$4,054 to forty-two physicians and \$948 to eighteen dentists for 2,054 hours of work in health centers. The Anti-Tuberculosis Association paid \$1,305 to five physicians for clinic sessions. With minor exceptions all other medical and preventive medical services were performed by physicians without remuneration.

#### DENTISTS

The participation of dentists in this study has been disappointing. Questionnaires were sent to all 148, but only 40.5 per cent replied. Many of these were incomplete.

The amount of charity work done by dentists cannot be estimated very closely, but on the basis of individual

TABLE 3.—*Total Charity Load of All Physicians and Dentists*

	Patients	
	Number	Distribution
Home and office practice.....	54,650	54.3%
Hospital inpatient practice.....	12,678	12.6%
Outpatient and clinic practice.....	33,251	33.1%
Total .....	100,579	100.0%
Cared for by physicians.....	88,131	87.6%
Cared for by dentists.....	12,448	12.4%

TABLE 4.—*Availability of Medical Care*

	Physicians and Dentists	
	Number	Per Cent
Present facilities and methods for providing medical care are adequate; no change indicated .....	32	21
More adequate provisions are needed to furnish medical, dental or hospital care to low income groups and to the indigent....	76	50
Other comments not pertinent to foregoing classification .....	45	29
Total .....	153	100

information it appears that the charity load of the individual physician is more than twice that of the individual dentist. The charity load of all physicians is probably more than eight times that carried by all dentists.

#### AVAILABILITY OF MEDICAL CARE

Of physicians and dentists commenting on the availability of medical care, 80 per cent knew of no instance in which persons had been unable to obtain medical,

dental or hospital care. Twenty per cent reported instances in which persons were unable to obtain such care.

The majority of physicians expressed some opinion regarding the adequacy or inadequacy of present methods and facilities for providing medical care. The

TABLE 5.—Charity Hospital Services

Hospital	Number of Indigent	Per Cent of Total
County Hospital .....	10,855	85.6
Children's Hospital .....	736	5.8
Norwood Hospital .....	350	2.8
Children's Home Hospital .....	232	1.8
Jefferson Sanatorium .....	225	1.8
St. Vincents Hospital .....	184	1.4
Salvation Army Hospital .....	71	0.6
West End Baptist Hospital .....	25	0.2

TABLE 6.—Services Performed by Nursing Organizations

	Nurses	Patients Served	Per Cent of Patients Served as Charity
Private duty nurses..... (Nurses' registry only)	208	5,712	0.8
Public health and visiting nurses			
Health department .....	41	22,187	100
Metropolitan Life .....	5	2,012	0
Total .....	208	29,911	55.7

interpretation of these opinions has been difficult, and for that reason the data should be regarded as only an approximation.

The most frequent comment made was an expression of the need for a part pay clinic and hospital for the low income group which would also provide for the specialized services such as x-ray and biopsy free or at reduced rates.

## HOSPITALS

There are in Jefferson County fourteen hospitals with a total capacity of 1,689 beds, or 3.5 beds per thousand of the population.

Hospital rates vary from a low of \$1.50 a day for ward beds to a high of \$10 a day for private rooms. These rates are not excessive.

Of a total of 41,000 patients cared for in local hospitals, 31 per cent were for charity. The average stay of pay patients in hospitals was 8.7 days, as compared to an average stay of 12 days for charity patients.

The load of charity hospital services was carried as shown in table 5.

Six hospitals operate outpatient departments or associated clinics and served 37,710 persons, of whom 18,081 were charity patients.

As regards inpatient services, most pay hospitals report the rejection of patients because of their inability to pay or because beds were not available. The number of persons rejected cannot be determined.

The County Hospital reports a need for 100 additional beds. All hospitals emphasize the need of providing for hospitalization of contagious diseases. As regards sanatorium beds for the treatment of tuberculosis there are now available for white persons only 72 per cent, and for Negroes only 5 per cent of those considered necessary for this county.

Group hospital insurance seems to have been an important factor in Jefferson County in making hospital care available to the general public, though there is no indication that it has served to lighten the load

of charity hospital service. Of an estimated number of 62,375 persons carrying hospital insurance providing complete or practically complete coverage, approximately 11,000 carry insurance through the Hospital Service Corporation and the remainder through various industrial arrangements.

## NURSING SERVICES

Services performed by the various nursing organizations may be summarized as in table 6.

The number of private duty nurses available through the nurses' registry, though small, appears adequate to serve those patients who can afford to pay for nursing services. There is one public health nurse for each 12,000 of the general population; accepted standards for good public health practice call for one nurse for each 2,500 of the population.

Nurses comment on the lack of provision for hospitalization of cases of contagious disease. Of a total of 3,653 contagious disease patients receiving some nursing care, 3 per cent were served by private duty nurses, the remainder by public health and visiting nurses. Approximately 65 per cent of the 22,187 individuals served by the health department nurses were clients of the department of public welfare.

## HEALTH DEPARTMENT

Time does not permit an adequate summation of the work of the health department; furthermore, the general familiarity of the profession with the nature of its services makes this unnecessary.

In 1937 the health department employed 113 persons in maintaining the following services: administration, records and vital statistics, laboratories, health education, food control, sanitation, child and maternal hygiene, public health nursing, and school health education.

Table 7 briefly outlines some of the major activities.

TABLE 7.—Major Activities of Health Department

1.	8,627 births and 5,892 deaths recorded 8,110 transcripts issued
2.	73,866 specimens (of value in the diagnosis of infectious diseases) were examined for physicians of Jefferson County 10,143 specimens of food and 3,087 samples of water from public water supplies examined The commercial value of this laboratory work by conservative estimate amounted to 1½ times the cost of operating the entire health department
3.	5,049 inspections of retail food establishments 171,758 veterinary inspections of animals slaughtered at packing houses 15,554 dairy inspections 230,000 pounds of food condemned 27,622 improvements effected
4.	22,685 sanitary inspections of public and private premises 6,670 nuisances abated 1,596 toilet facilities improved or installed 631 cases of contagious diseases isolated 1,732 contacts quarantined
5.	954 public lectures given 1,132 moving pictures shown 52 radio talks given
6.	53,804 visits by nurses to 22,187 persons 12 maternal and child hygiene, and 4 dental clinics operated serving 8,070 persons who were seen by physicians or dentists

The health department is well organized and its activities are well conducted. Its usefulness, however, is greatly limited through lack of funds. The committee does not feel that a detailed report of the financial needs of the health department is pertinent to the present discussion except to state (1) that expenditures for public health in Jefferson County are not only small but fall more than 50 per cent short of the



requirements for a minimum program which may be consistent with safety and (2) that, while state subsidy to Jefferson County for county health work has increased in recent years, such subsidy on a per capita basis is still only 50 per cent of that allocated to other counties and should be increased.

A detailed discussion of the financial status of the health department has been submitted to the board of censors for its information and for such action as it may deem appropriate.

#### PRIVATE AND GOVERNMENTAL WELFARE, RELIEF AND UNOFFICIAL HEALTH AGENCIES

Of the thirty-seven agencies included in the category of private and governmental welfare, relief and unofficial health agencies, twenty-seven are financed by the community chest. Fourteen agencies either arrange for or furnish medical or dental care. Ten arrange for or provide care in physicians' or dentists' offices, while six arrange for or provide care in the home. Eleven agencies attempt to arrange for hospital services, though none should be considered as actually doing so as most hospitals have their own rules for accepting patients regardless of who may refer them for care. Seven agencies provide limited supplies of drugs.

Clinics are maintained as shown in table 8.

TABLE 8.—Clinics Maintained by Agencies

	Number of Visits *
Department of public welfare.....	1,890
Antituberculosis association .....	3,911
Fresh air farm.....	350
Juvenile court .....	1,500
Trinity community house.....	3,131
Total clinic visits.....	10,782

\* All numbers are estimated

Those agencies which operate clinics render a direct service. Most others seek medical care for their clientele by requesting physicians to render services without charge or by utilizing other charity institutions. The more important charity organizations which carry the great bulk of the charity load, and which are most commonly utilized by all the various agencies are the antituberculosis association, children's hospital and clinic, county hospital and clinic and the health centers of the health department.

It is estimated that approximately 7,100 persons were provided with care through direct efforts of all the various social agencies. They report a total of 1,270 persons for whom care could not be obtained; 1,100 of these were reported by the department of public welfare.

#### DEPARTMENT OF PUBLIC WELFARE

Because of its importance, special mention should be made of the department of public welfare. During the year 1937 the department averaged approximately 4,000 families who received financial assistance. These were made up of those over 65 years of age, households with children under 16 where there was no employable head of the family, and those entirely physically or mentally handicapped to earn a living. The case load represents a high percentage of individuals having physical disabilities.

Because of limited funds, appropriations for prescriptions, drugs, visits of physicians and medical appliances must all be kept on the same inadequate basis as the

monthly grants, which in their entirety are below the subsistence level for food.

A total of \$1,308 of city-county funds was expended for maintenance of a medical office in Birmingham, while \$1,585 in city-county funds was expended in maintaining a clinic in Bessemer; to the latter the Works Progress Administration added \$3,911. The total expenditures by the department of public welfare (from all sources) was \$6,804 for the medical care of the sick in 4,000 families. Of this total physicians received \$289.

Provisions for home and office visits of physicians are for emergency cases only and are entirely inadequate to meet the medical needs of persons on relief. The clinic facilities in Bessemer are, of course, available only to persons on relief who live in that district. Under the circumstances it is not surprising that medical care was not obtained for an estimated number of 1,100 persons.

#### SCHOOLS

There are six school systems with a total enrolment of 103,000. Two systems with approximately half this enrolment provide for medical and dental inspection of pupils. In the other four systems the health status of the child rests with the teacher or public health nurse, and arrangements for medical examination and care must be made through family physicians, clinics, health centers or other means as circumstances permit. One failure of existing school health programs lies in the inability to make medical examinations at regular intervals. As a result many defects which might be corrected through private or public means are never discovered. Furthermore, facilities are not available to follow up properly those children who need corrections in an effort to see that they are obtained.

#### MEDICAL CARE IN INDUSTRIES

Forty-nine establishments provide medical care of employees only in case of accidents. Twenty-two firms furnish complete medical care for approximately 190,000 employees and dependents. With minor exceptions medical care provided by industries is judged to be adequate. Of the employees of all companies which provide complete medical care, 92.3 per cent have free choice of physician and may elect medical care by fee deduction or in two instances may accept such services from the company without cost to themselves. Approximately 2,900 individuals are given medical care through mutual benefit associations or by similar arrangements.

#### PHARMACISTS

The reports from pharmacists are not sufficiently reliable to merit attention. Of interest, however, was their comment regarding the needs for medical care.

Of seventy-nine pharmacists making comment, four considered present facilities for medical care adequate; three made miscellaneous comment. Seventy-two favored a change in methods or facilities for providing medical care and thirty-two of these favored some unspecified form of governmental control, four advocated utilization of the community chest, while thirty-six offered no plan or suggestion.

#### NEEDS FOR MEDICAL CARE

Physicians and dentists in home, office and institutional practice, on very conservative estimate, cared for from 100,000 to 116,000 charity patients. Despite this tremendous charity load carried by the professions, it

appears that present facilities are inadequate and that many needy persons were unable to obtain medical care.

The actual number of persons unable to obtain such care cannot be determined with accuracy. What is perhaps more important than arriving at the actual number is an appreciation of those circumstances under which medical care is ordinarily not available.

There is no great difference of opinion between physicians, dentists and the various social and health agencies as to the inadequacies of facilities and the present circumstances under which medical care is not available. These inadequacies are expressed in the following recommendations made by these groups in answering questionnaires.

The most commonly expressed opinions of physicians, dentists and the various social agencies for additional needs are:

1. Part pay clinics and hospital for the low income group.
2. Dental clinics (performing preventive and restorative services for the indigent).
3. Provisions for home care of the indigent and follow-up care of those discharged from hospitals. Also ambulance service to charity hospitals for the critically ill.
4. Better facilities for the treatment of syphilis.
5. Provision for hospitalization of contagious disease cases.
6. More sanatorium beds for the treatment of tuberculosis.
7. More adequate provision for the care of transients and nonresidents.
8. Increased facilities at Hillman Hospital and clinic, larger social service staff.
9. Increased facilities of health department.

The various agencies also expressed the following opinions which were not commonly expressed by members of the professions. Need for:

1. Payment through public funds of physicians and dentists for home, office and institutional care of the indigent.
2. A centralized social service bureau to serve all agencies.
3. Provision for health examination of persons over 12 years of age.

4. Psychiatric clinics; more adequate hospital provisions by the state for the care of mental cases.
5. More adequate provision for drugs, teeth, eyeglasses and so on.
6. Child guidance clinic.
7. Ear clinic for the treatment and prevention of hearing defects.
8. Better organization of medical resources.

#### RECOMMENDATIONS

1. The committee endorses in principle a part pay hospital and clinic for the low income group, which group it designates as those whose income level is just above that established by the Hillman Hospital in its "basic guide for determining indigency."

2. In order to differentiate between charity, part-pay and pay patients the committee feels that it will be essential to establish a dignified and efficient business bureau with a social service department to investigate thoroughly the financial status of patients. This should be a centralized service functioning for all charity and part-pay institutions including the Hillman Hospital and clinic, department of public welfare, health department and others.

3. The committee recognizes the total inadequacy for hospital care of cases of contagious disease (both pay and indigent) and feels that some provision should be made.

4. The committee feels that local appropriations for public health in Jefferson County are not only small but fall 50 per cent short of the requirements for a minimum program. Furthermore, state subsidy to Jefferson County for county health work, on a per capita basis, is only 50 per cent of that granted to other counties and should be increased.

[The remainder of the report deals with a local hospital and a special "Proposed Plan for the Medical Care of the Indigent and Low Income Groups."]

## OFFICIAL NOTES

### JUDGE PROCTOR OVERRULES MOTION TO QUASH SECOND SUBPENA

Following Judge James M. Proctor's quashing of two thirds of a subpoena requiring the American Medical Association to present before the Special Grand Jury certain records, some extending as far back as sixteen years, the Department of Justice revised the subpoena. The revised subpoena would command to bring: All . . . documentary communications and all reports or memoranda . . . containing statements with respect to any action or policy taken or adopted or considered or proposed to be taken or adopted by or on behalf of the A. M. A. or of any medical society or association affiliated with the A. M. A., or of any hospital, in opposition to group medical practice or to the provision of medical care on a periodic prepayment basis, drawn up, sent or received from Jan. 1, 1935, to Nov. 20, 1938, by certain officials at the headquarters of the association, its judicial council, its bureau of investigation, and any other official employee of the association who, according to the present knowledge of the officials, drew up, sent or received such papers.

Counsel for the American Medical Association argued before the court that the present order was so broad that it was void. Counsel also quoted a decision by Justice Holmes of the United States Supreme Court to the effect that it was "contrary to first principles of justice" for a grand jury to go deeply into records of a corporation "in the hope that something will turn up."

In overruling the motion to quash the revised subpoena, Justice Proctor is reported to have set down the following memorandum opinion:

A recent subpoena duces tecum to the American Medical Association was partially quashed, as unreasonable and oppressive because of its sweeping requirements. This subpoena is intended to overcome those faults. I think it does so.

The desired papers are well identified. The periods of time to be covered by the search, although longer than the statutory period of limitation, are definitely fixed, and not necessarily unreasonable, having in mind the nature of the inquiry. The papers required, it is understood, are only those which may now be in possession of the association or its officers.

I see no reason why the association cannot comply with the subpoena without undue difficulty or hardship, if its papers have been kept under any efficient system of filing.

Counsel for the association again contend that the papers described by the subpoena are irrelevant and incompetent to the subject matter of the inquiry before the grand jury and that the matters being investigated cannot by their nature involve any violation of the Sherman Antitrust Act, in respect of its local or interstate provisions. It is therefore argued that as the investigation concerns matters of which this court would have no jurisdiction, the proceeding cannot legally form the foundation for issuance of the subpoena. It is insisted that the court should now determine these basic questions.

I cannot agree with these contentions. The virtual effect of the propositions to now pass upon the admissible quality of evidence sought for production before the grand jury, or produced before it, and to determine vital questions of jurisdiction, would be to require a close and detailed supervision by the court of the grand jury process in this investigation which, I think, can find no proper support in the historical background and development of the grand jury system, or the well established rules of criminal procedure. Moreover, the present inquiry before the special

grand jury is of an original nature. Neither the American Medical Association nor any other party has been held for action of the grand jury upon any criminal charge. The inquisition has its origin with the grand jury. There are as yet no defendants. There may never be any. Hence, at this stage of the proceedings, the association has no such status as entitles it to raise any of the vital questions now urged upon the court.

In my opinion, the motion to quash the subpoena should be overruled, and it is so ordered.

## ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

The Annual Congress of the Council on Medical Education and Hospitals of the American Medical Association will be held at the Palmer House, Chicago, Feb. 13 and 14, 1939. The Federation of State Medical Boards of the United States will participate in the Congress. The program follows:

### MONDAY MORNING, FEBRUARY 13

*The Protection of the Public Through the Activities of the Council on Medical Education and Hospitals*

Ray Lyman Wilbur, M.D., LL.D., Chairman, Stanford University, Calif.

(Subject to be Announced)

James B. Conant, Ph.D., President, Harvard University, Cambridge, Mass.

*The Organization and Subject Matter of General Education*

Robert Maynard Hutchins, LL.B., President, University of Chicago.

(Subject to be Announced)

Walter F. Donaldson, M.D., Secretary, Medical Society of the State of Pennsylvania, Pittsburgh.

*Canadian Experiments in Medical Economics*

T. C. Routley, M.D., LL.D., General Secretary, Canadian Medical Association, Toronto, Ont.

### MONDAY AFTERNOON, FEBRUARY 13

*The South as Testing Ground for the Regional Approach to Public Health and Public Welfare*

Howard W. Odum, LL.D., Director, Institute for Research in Social Science, University of North Carolina, Chapel Hill.

### SYMPOSIUM ON THE SMALL HOSPITAL

*Organization and Management of the Small Hospital*

Malcolm T. MacEachern, M.D., Associate Director, American College of Surgeons, Chicago.

*The Community Hospital*

Barry C. Smith, General Director, The Commonwealth Fund, New York.

*The Planning and Organization of the Small Hospital*

William Henry Walsh, M.D., Consultant Specialist on Hospitals, Chicago.

*The Construction of the Small Hospital*

Carl A. Erikson of the firm of Schmidt, Garden and Erikson, Architects, Chicago.

### TUESDAY MORNING, FEBRUARY 14

*The Program of the National Committee for Mental Hygiene*

Clarence M. Hincks, M.D., General Director, National Committee for Mental Hygiene, New York.

*Federal Support of Professional Education*

Dean Lewis, M.D., Surgeon-in-Chief, Johns Hopkins Hospital, Baltimore.

*Fundamentals of Industrial Hygiene*

T. Lyle Hazlett, M.D., Professor of Industrial Hygiene, University of Pittsburgh School of Medicine and Medical Director, Westinghouse Electric and Manufacturing Company, Pittsburgh.

*The Relation of Anesthesiology to Medical Education*

Ralph M. Waters, M.D., Department of Anesthesia, University of Wisconsin Medical School, Madison.

*Tenure of Members of the Faculty in Schools of Medicine*

Anton J. Carlson, Ph.D., Frank P. Hixon Distinguished Service Professor of Physiology, University of Chicago.

### TUESDAY NOON, FEBRUARY 14

Luncheon meeting, to which all those attending the Congress are invited to attend:

Address: *What the Undergraduate College Should Give the Future Doctor*

William Mather Lewis, LL.D., President, Lafayette College, Easton, Pa.

### MONDAY EVENING, FEBRUARY 13

#### FEDERATION DINNER

(Program to be announced later.)

### TUESDAY, FEBRUARY 14

THE FEDERATION OF STATE MEDICAL BOARDS OF THE  
UNITED STATES

(Program to be announced later.)

## THE ST. LOUIS SESSION

### Special Exhibits on Fractures and on Anesthesia in the Scientific Exhibit

The Committee on Scientific Exhibit of the Board of Trustees has announced two special features for the St. Louis session, May 15-19, 1939.

The Special Exhibit on Fractures will be presented as a former annual sessions under the supervision of a committee the members of which are Dr. Kellogg Speed, Chicago, chairman; Dr. Frank D. Dickson, Kansas City, Mo., and Dr. Walter Estell Lee, Philadelphia.

The Special Exhibit on Anesthesia will be presented for the third year under the supervision of a committee composed of Dr. Ralph M. Waters, Madison, Wis., chairman; Dr. John S. Lundy, Rochester, Minn.; Dr. Henry S. Ruth, Philadelphia, and Dr. Philip D. Woodbridge, Boston.

Application blanks for space for other exhibits may be obtained from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago.

## COMMITTEE OF PHYSICIANS MAKES NEW RELEASE

The Committee of Physicians for the Improvement of Medical Care, Inc., issued for release on December 3 a statement signed by Dr. John P. Peters and said to express the point of view of the committee in relationship to the National Health Program.

## WITNESSES BEFORE THE GRAND JURY IN WASHINGTON

The following additional witnesses are reported to have appeared before the Special Grand Jury in Washington, D. C.: Dr. Harry Clifford Loos of the Ross-Loos Medical Group, Los Angeles, and Dr. George R. Stevenson of the San Diego Beneficial Society, San Diego, Calif. Dr. Michael A. Shadid of Elk City, Okla., said to be the founder and medical director of the Farmer's Union Cooperative Hospital Association, and Mr. F. D. Kilpatrick, said to be a labor leader of Akron, Ohio, who is organizing the Summit County Cooperative Health Association.

## RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company, entitled "Your Health," began Wednesday October 19 and will run consecutively for thirty-six weeks.

The program is broadcast each Wednesday over the Blue network of the National Broadcasting Company at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).<sup>1</sup>

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

- December 14. What Shall We Eat?
- December 21. Hidden Treasures in Foods.
- December 28. Good Milk, Good for You.

1. Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.

## Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

### ARIZONA

**Plague Infection in Prairie Dogs.**—According to *Public Health Reports*, plague infection has been proved in a pool of ninety-eight fleas collected from eighteen prairie dogs (*Cynomys gunnisoni zuniensis*) shot September 27 seven miles south of St. Johns, Apache County.

### ARKANSAS

**Seventeenth Clinical Meeting.**—The Fort Smith Clinical Society held its seventeenth meeting in Fort Smith October 11 under the auspices of the clinical staffs of St. Edwards Mercy and Sparks Memorial hospitals. The speakers included:

- Dr. George V. Brindley, Temple, Texas, Treatment of Acute Perforated Appendicitis and Peptic Ulcer, Its Complications and Indications for Surgical Treatment.
- Dr. Sidney J. Wolfemann, The Advantages of Vitallium in Bone Fixation.
- Dr. William R. Brooksher, The Painful Shoulder.
- Dr. Paul M. Bassel, Temple, Thyroid Dysfunction.
- Dr. Charles T. Chamberlain, The Heart and Obesity.
- Dr. James H. Buckley, Differential Diagnosis of Acute Conjunctivitis, Iritis and Glaucoma.
- Dr. Arless A. Blair, Treatment of Underweight in Nondiabetic Individuals with Protamine Zinc Insulin.
- Dr. James W. Amis, Use of Sulfanilamide in Undulant Fever.
- Dr. Arthur F. Hoge, Factors in Mortality of Appendicitis.

### COLORADO

**Midwinter Graduate Clinics at Denver.**—The midwinter graduate clinics, sponsored by the Colorado State Medical Society, will be at the Shirley-Savoy Hotel, Denver, December 14-16. The clinics are open to all doctors of medicine in the Rocky Mountain region regardless of membership in any medical society. The guest speakers will include:

- Dr. Arlie Ray Barnes, Rochester, Minn., professor of medicine, University of Minnesota Graduate School of Medicine.
- Dr. Rollin Russell Best, Omaha, Neb., assistant professor of anatomy and surgery, University of Nebraska School of Medicine.
- Dr. Horton Ryan Casparis, Nashville, Tenn., professor of pediatrics, Vanderbilt University School of Medicine.
- Dr. Everett Dudley Plass, Iowa City, professor of obstetrics and gynecology, State University of Iowa College of Medicine.
- Dr. James E. M. Thomson, Lincoln, Neb.

### ILLINOIS

**Tri-County Meeting at Galesburg.**—The Knox County Medical Society was host at a meeting with the Henry and Warren county medical societies in Galesburg October 25. The speakers included:

- Dr. Warren H. Cole, Chicago, Hyperthyroidism.
- Dr. Claire LeRoy Straith, Detroit, First Aid Treatment of Automobile Injuries to the Face.
- Dr. William P. Murphy, Boston, The Practical Management of the Anemic Patient.
- Dr. Arthur E. Hertzler, Halstead, Kan., as the after dinner speaker, discussed "Hooks, Bobs and Sinkers." Dr. Logan Clendening, Kansas City, also spoke.

### Chicago

**Hospital News.**—The National Jewish Hospital, a tuberculosis sanatorium, Denver, has recently established an office in Chicago at 30 North La Salle Street.

**Personal.**—Dr. Paul R. Cannon, professor of pathology, University of Chicago, has been appointed a member of the Medical Fellowship Board of the National Research Council, for the period ending June 30, 1941, to complete the unexpired term of Dr. Eugene L. Opie, New York, who resigned.

**Society News.**—At a meeting of the Chicago Neurological Society October 20 the speakers were Drs. Foster Kennedy, New York, on "The Organic Background of Mind"; Victor E. Gonda, "War Neuroses," and Paul C. Bucy, "Tremor: A Consideration of Its Physiology and Abolition by Surgical Means."—The Chicago Ophthalmological Society was addressed October 24 by Drs. Samuel G. Higgins, Milwaukee, on "Ophthalmic Surgery in India" and William A. Fisher, "Senile Cataract: The Usual Method of Operating in India." Dr. Robert von der Heydt showed photographs in color of diseases of the eye.—Dr. Howard C. Taylor Jr., New York, discussed "Relationship of Hormones to the Toxemias of Pregnancy" before the Chicago Gynecological Society November 18.

—The Chicago Orthopaedic Society was addressed November 11 by Drs. Walter R. Fischer on "Fracture of the Scapula Requiring Open Reduction" (report of a case) and Wallace H. Cole, St. Paul, "Clinical Observations on the Physiology of Bone."—Dr. Gilbert J. Thomas, clinical associate professor of urology, University of Minnesota Medical School, Minneapolis, discussed "Tuberculosis of the Urological Tract" before the Chicago Medical and Urological societies at a joint meeting December 7 at the Chicago Woman's Club.

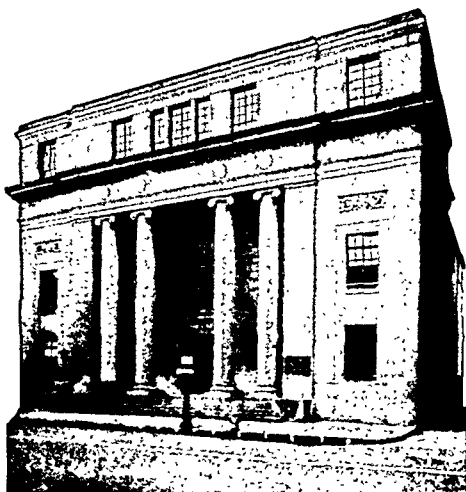
### IOWA

**Personal.**—Rev. G. T. Notson resigned as superintendent of the Methodist Hospital, Sioux City, October 21; he has held the position since the hospital was founded eighteen years ago.—Dr. Edward N. Anderson, Boston, has been appointed head football coach at the State University of Iowa, Iowa City, following his resignation from a similar position at Holy Cross College, Boston. Dr. Anderson graduated at Rush Medical College in 1930.

**Gifts to the University.**—The University of Iowa College of Medicine, Iowa City, announces a gift of \$22,500 from the John and Mary R. Markle Foundation to be spent over a two year period. Of the total, \$12,500 will provide for a continuation of the research in the department of ophthalmology under Dr. Cecil S. O'Brien on inflammatory conditions of the eye, and the remainder will be used to continue the research program in the department of pathology under Dr. Harry P. Smith, on blood clotting and the bleeding tendency.

### KENTUCKY

**Memorial to Dr. Joseph N. McCormack.**—Headquarters of the Kentucky State Medical Association and the State Department of Health of Kentucky were recently moved to a new home purchased by the state at 620 South



Home of State Medical Association and State Department of Health.

Third Street, Louisville, and dedicated October 4 during the annual meeting of the state medical association. The building has been made a permanent memorial to Dr. Joseph N. McCormack, first health officer of the state. Speakers at the dedicatory exercises were Drs. Carl C. Howard, Glasgow, former president of the state association, on "Joseph Nathaniel McCormack the Physician"; Gov. Albert B. Chandler, "Joseph Nathaniel McCormack the Public Servant," and Dr. Arthur T. McCormack, state commissioner of health, secretary of the state medical association and son of the elder McCormack. After the governor's address Miss Mary Tyler McCormack unveiled a portrait and a bronze plaque of her grandfather in the entrance hall of the building. The portrait was painted by Charles Sneed Williams, a Kentucky artist, and presented by the medical association. The plaque was the gift of the state department of health and of county health departments. Dr. Joseph N. McCormack was appointed state health officer when the state board of health was created in 1883 following an epidemic of yellow fever. He is said to have been instrumental in the passage of the state's first medical practice act and the first administrator of the law. Among other laws he sponsored were licensure laws, a vital statistics law and a bill

consolidating health agencies. He was chairman of the committee on reorganization of the American Medical Association, which functioned from 1901 to 1910. Dr. McCormack died Aug. 4, 1922, aged 75.

### MICHIGAN

**Hospital News.**—Dr. Roscoe R. Graham, Toronto, lectured at Woman's Hospital, Detroit, Hospital Day, November 9; his subject was "Some Philosophic Problems Dealing with the Relation of the Fundamental Sciences to Every Day Surgical Problems."

**Personal.**—A testimonial dinner was held in honor of Drs. Rudolph J. Maas and William P. Scott, Houghton, by the Hancock Council of the Knights of Columbus, Hancock, October 11. Dr. Maas is 83 years old and a charter member of the council; Dr. Scott is 80, a charter member of the Houghton County Medical Society and an emeritus member of the Michigan State Medical Association.

**Society News.**—A symposium on ovarian tumors was presented before the Ingham County Medical Society in Lansing October 18 by Drs. Harry M. Nelson and Donald C. Beaver, Detroit. —Dr. Evan G. Galbraith, Toledo, discussed "Pulmonary Atelectasis" before the Jackson County Medical Society in Jackson October 18. —Dr. Harry A. Towsley, Ann Arbor, addressed the Washtenaw County Medical Society October 11 on "The Acute Exanthemata." —Dr. Thurman B. Rice, Indianapolis, discussed "New Concepts in Bacteriology" before the Muskegon County Medical Society in Muskegon October 28.

**Thirteenth Annual Highland Park Clinic.**—The thirteenth annual clinic of the Highland Park Physicians Club was held November 30 at the Highland Park General Hospital. The following program was presented:

Dr. James R. Goodall, Montreal, The Placental Blood Bank.  
Dr. Eugene H. Shannon and J. A. Sullivan, M.B., Toronto, Clinical and Radiologic Aspects of Diseases of the Paranasal Sinuses.  
Dr. Russell L. Haden, Cleveland, Treatment of Anemia.  
Dr. Frederick Christopher, Evanston, Ill., Carcinoma of the Stomach.  
Dr. Martin H. Fischer, Cincinnati, Clinical Aspects of Water Turnover.

Dr. Henry A. Luce, Detroit, president of the Michigan State Medical Society, was toastmaster at the annual banquet and Malcolm W. Bingay, editorial director, *Detroit Free Press*, was the speaker.

### MISSISSIPPI

**Society News.**—The Delta Medical Society was addressed in Indianola October 12, among others, by Drs. Randolph T. Smith, Little Rock, Ark., on "Unusual Tumors of the Ovary" and Bernard H. Booth, Drew, "Atrabrine in Malaria." —A symposium on diseases of nutrition was presented before the Issaquena-Sharkey-Warren Counties Medical Society in Vicksburg October 11 by Drs. Henry B. Goodman, Anguilla; George W. Gaines, Tallulah, La.; Hugh H. Johnston, Vicksburg, and Walter H. Scudder, Mayersville.

### NEW JERSEY

**Cooperative Child Guidance Program in Paterson.**—A child guidance program centered about the neuropsychiatric clinic of the Paterson General Hospital has been developed in cooperation with interested agencies. The plan is to have a discussion with the specific agency that can best aid each child, with suggestions for treatment. A monthly conference is planned with each agency to study the development of the child, who is seen frequently at the clinic during the period of study. The general hospital gives its facilities to the project, and the social agencies contribute the social workers and social facilities. Among the agencies that are cooperating are the Family Welfare Society, probation authorities, criminal courts, police department, schools, churches, Church Mission Help, North Jersey Training School, the Young Men's Christian Association, Young Women's Christian Association, the Young Men's Hebrew Association and Young Women's Hebrew Association. Dr. Theodore Rothman is director of the project.

**Society News.**—At a recent meeting of the Monmouth County Medical Society in Asbury Park the speakers were Drs. Harold A. Kazmann, Long Branch, on "Early Symptoms of Gastrointestinal Carcinoma"; Louis F. Albright, Spring Lake, "Treatment of Pernicious Anemia," and Carlos A. Pons, Asbury Park, "Rocky Mountain Spotted Fever." —A symposium on pain low in the back was presented before the Passaic County Medical Society in Passaic October 13 by Drs. Arthur Bruce Gill, Philadelphia; William J. Mixer, Boston, and Samuel Kleinberg, New York. —Dr. Frederic E. Elliott, Brooklyn, addressed the Essex County Medical Society, Newark, November 10, on "Medical Expense Insur-

ance." —Dr. Jesse G. M. Bullowa, New York, addressed the Bergen County Medical Society, Bergen Pines, November 8, on "The Pneumonias." —Dr. Samuel A. Loewenberg, Philadelphia, addressed the Academy of Medicine of Northern New Jersey, Newark, November 17 on "Endocrine Disturbances and Present Day Endocrine Therapy."

**Committee on Health and Welfare Appointed.**—Gov. A. Harry Moore has appointed a special committee to "follow up and determine applications to the needs of New Jersey of certain of the considerations brought out at the Washington Conference in July." It will be known as the New Jersey Committee on Health and Welfare. Robert C. Clothier, L.L.D., president of Rutgers University, New Brunswick, is general chairman of the committee, which has fifty members, including twenty-five physicians. Six technical subcommittees were created at the organization meeting in Trenton, November 16, as follows: expanded public health facilities, hospital facilities, indigent, low wage, wage loss insurance and related matters. Twelve advisory committees to the subcommittee on expanded public health facilities were also created, as follows: advisory committee at large, maternal and child health, crippled children, blind, tuberculosis, venereal disease, cancer, pneumonia, mental diseases, industrial diseases, school health and college health.

Complete, comprehensive information on all phases of medical care in New Jersey will be assembled by this committee. The fact-finding work of the committee will include determination of what physical equipment, facilities and services are available to satisfy the health requirements of the population, determination of the incidence of degenerative diseases, among groups in various income levels, determination of the adequacy of present sanitation measures and determination of what additional physical equipment, facilities, services and policies are required to assure that the health of the people will be safeguarded. Finally the committee will undertake to develop practical methods for remedying any conditions or deficiencies amenable to improvement. In the collection of this information, data accumulated in the surveys conducted by the Medical Society of New Jersey and its component county medical societies will be utilized for information on those phases of medical care which they cover.

The following physicians are members of the committee: Drs. William J. Carrington, Atlantic City, president of the state medical society; Fred H. Albee, New York; Walter G. Alexander, Orange; Leverett D. Bristol, Montclair; Charles V. Craster, Newark; Samuel B. English, Glen Gardner; George W. Fithian, Perth Amboy; Edward Guion, Northfield; Edgar A. Ill, Newark; Allen G. Ireland, Trenton; Henry Kessler, Newark; Joseph H. Kler, New Brunswick; Augustus H. Knight, Far Hills; Frederick P. Lee, Paterson; Julius Levy, Trenton; Jesse Lynn Mahaffey, Trenton; Stanley H. Nichols, Asbury Park; George O'Hanlon, Jersey City; Berthold S. Pollak, Secaucus; Ellen C. Potter, Trenton; Hilton S. Read, Atlantic City; Joseph M. Rector, Jersey City; Spencer T. Snedecor, Hackensack; Arthur L. Stone, Camden, and LeRoy A. Wilkes, executive officer of the state medical society.

### NEW YORK

**Rochester Academy Plans Museum.**—Plans for a medical museum in the new building of the Rochester Academy of Medicine are in process of formation. Committees have been formed to develop divisions dealing with rare books and documents, plastic and graphic arts, instrument making and historical development, and pathologic anatomy. Courses of instruction for the committees have been arranged with the librarians of the city, and the university and the Rochester Museum of Arts and Sciences is cooperating. The academy wishes especially to compile the medical history of Monroe County. Dr. Morris E. Missal is secretary of the museum committee.

### New York City

**Third Harvey Lecture.**—Dr. Eugene F. Du Bois, professor of medicine, Cornell University Medical College, will deliver the third Harvey Lecture at the New York Academy of Medicine December 15 on "Heat Loss from the Human Body."

**Faculty Appointments.**—New York Medical College and the Flower Hospital recently announced the appointment to the faculty of Dr. Reuel A. Benson to be professor of pediatrics, James W. Benjamin, Ph.D., associate professor of histology, embryo and neuroanatomy, and Dr. David Scherf, associate clinical professor of medicine. Dr. Benjamin was formerly assistant professor of zoology at Northwestern University, Chicago, and Dr. Scherf was associate professor of medicine at the University of Vienna.

**Hospital News.**—A department of anesthesiology was recently opened at the Evangelical Deaconess Hospital with Drs. Henry Trautmann and Harry J. Rosenthal in charge. —The name of the Brooklyn Home for Consumptives is to be changed to the Brooklyn Thoracic Hospital. —The Frances Schervier Hospital and Home for the Aged, built by the Sisters of the Poor of St. Francis, was dedicated November 6. It is a six story building with 404 beds. The first patients were those formerly in the St. Francis Home for Aged Incurables. —A new wing of St. Clare's Hospital was dedicated October 30.

**Society News.**—A symposium on serum therapy in pneumonia was presented at the stated meeting of the New York Academy of Medicine December 1 by Drs. Russell L. Cecil, Colin M. MacLeod and Wheelan D. Sutliff. —A program on pneumonia was presented before the Bronx County Medical Society November 16 by Drs. Ralph S. Muckenfuss, John A. Colucci, Jesse G. M. Bullova and Colin M. MacLeod. —Dr. James T. Gwathmey addressed the Bronx Pathological Society November 15 on "Pathology of Anesthesia: Tissue Changes and the Pathologic Physiology Involved in the Use of Modern Anesthetics." —A pneumonia program was presented before the Medical Society of the County of Queens November 1 by Drs. Wheelan D. Sutliff on "The New York City Pneumonia Control Program"; Carl Boettiger, Flushing, "Early Diagnosis of Pneumonia"; Rufus I. Cole, Mount Kisco, "Serum Therapy of Pneumonia," and Colin M. MacLeod, "Antipneumococcic Rabbit Serum Therapy of Pneumonia." Dr. Alfred C. Beck addressed the society October 25 on "Syphilis in Pregnancy."

### NORTH CAROLINA

**Special Society Meetings.**—Drs. Burton Haseltine, Chicago, and Grady E. Clay, Atlanta, addressed the North Carolina Eye, Ear, Nose and Throat Society at its annual meeting in Raleigh recently on "Chronic Sinus Infections" and "Arteriolar Changes in the Fundus Oculi; Convergent Strabismus in Children" respectively. Dr. Franklin C. Smith, Charlotte, was elected president; Dr. Henry H. Briggs Jr., Asheville, vice president, and Dr. Milton R. Gibson, Raleigh, reelected secretary. —Dr. Vann M. Long, Winston-Salem, was elected president of the North Carolina Urological Association at its annual meeting in Greensboro October 31. Dr. John Mason Hundley Jr., Baltimore, was the guest speaker at the annual dinner, on "Physiologic and Pathologic Observations on the Urinary Tract During Pregnancy."

### OKLAHOMA

**New Health Officers.**—Dr. Frederick E. Dargatz, formerly of Kinsley, Kan., has been appointed director of the health unit of Ardmore to succeed Dr. Richard M. Parish. —Dr. Reed Wolfe, Sulphur, has been appointed health superintendent of Choctaw County.

**Society News.**—Drs. Carroll M. Pounders, Oklahoma City, and James William Finch, Hobart, addressed the Western Oklahoma Medical Society at a meeting in Hobart recently on "Rheumatic Fever in Childhood" and "Etiology of Nausea and Vomiting of Pregnancy" respectively. —Drs. J. Wendall Mercer and Evans E. Talley, Enid, addressed the Woods-Alfalfa County Medical Society, Cherokee, recently on "Prenatal Disturbances, Symptoms and Treatment" and "The Thyroid" respectively. —Drs. Rufus Q. Goodwin and Frederick Redding Hood, Oklahoma City, addressed the Garfield County Medical Society, Enid, October 27, on "Treatment of Pneumonia with Serum Therapy" and "Cardiac Irregularities" respectively.

### PENNSYLVANIA

**Program on Exceptional Child.**—The child research clinic of the Woods Schools, Langhorne, presented its fifth institute on the exceptional child October 18. The following program was given:

Dr. Eugenia S. K. Cameron, Baltimore, Factors in the Etiology of Psychoses in Early Adolescence.  
Dr. Lawson G. Lowrey, New York, Problems of Aggression and Hostility in the Exceptional Child.  
Dr. Josephine H. Kenyon, New York, Stimulation of Growth in Short Children.  
Edgar A. Doll, Ph.D., Vineland, N. J., Social Maturation.  
May Ayres Burgess, Ph.D., New York, Height Charts in Growth Studies.

Dr. Frederick H. Allen, Philadelphia, presided at the morning session and Miles Murphy, Ph.D., Philadelphia, at the afternoon session.

### Philadelphia

**Plans for Third Postgraduate Institute.**—The Philadelphia County Medical Society will sponsor its third annual Postgraduate Institute March 13-17, 1939, on the subjects "Blood Dyscrasias" and "Metabolic Disorders." There will be eighty-six clinical lectures with open forum discussion of each topic. Dr. Rufus S. Reeves is director of the institute. Sessions will be held at the Bellevue-Stratford Hotel.

**Society News.**—Dr. William Bates addressed the Philadelphia Clinical Association November 15 on "Pseudosurgical Abdomen." —At a meeting of the Philadelphia Neurological Association November 18 the speakers included Drs. Lester S. King, Princeton, N. J., on "Equine Encephalomyelitis" and George D. Gammon, "The Muscular Weakness of Family Periodic Paralysis." —Members of the department of diseases of children, Columbia University College of Physicians and Surgeons, New York, addressed the Philadelphia Pediatric Society November 8. Among the speakers were Drs. John P. Caffey, on "Syphilis of the Skeleton in Early Infancy; the Nonspecificity of Many of the Roentgen Changes," and Richard L. Day, "Effect of Sleep on Insensible Perspiration in Infants and Children."

**Women Sponsor Cancer Forum.**—The Women's Auxiliary of the Lankenau Hospital Research Institute and district 1 of the Pennsylvania State Nurses' Association sponsored a cancer forum November 29-30 at the Bellevue-Stratford. The guest speakers included:

Dr. William B. Wartman, Cleveland, Highlights in the History of Cancer.  
Dr. James J. Durrett, U. S. Food and Drug Administration, Washington, D. C., Cancer Quacks.  
Dr. Martha Edith MacBride-Dexter, Harrisburg, state secretary of health, Activities of the Pennsylvania Department of Health with Special Reference to Cancer.  
Dr. William Carpenter MacCarthy, Rochester, Minn., How the Pathologist Aids in Combating Cancer.  
Major Julia C. Stimson, Army Nurse Corps, U. S. Army, retired, New York, The Nurses' Responsibility in Prevention and Early Recognition of Cancer.

### Pittsburgh

**Hospital News.**—Montefiore Hospital held its annual "scientific day" November 12 with Dr. Samuel A. Levine, Boston, as the guest speaker and clinician. Dr. Levine spoke in the evening on "The Value of Auscultation."

**Research on Air Filters.**—Mellon Institute announces the establishment of an industrial fellowship by the American Air Filter Company, Louisville, Ky., for the study of materials of value in the construction of filters for air conditioning systems. Frank F. Rupert, Ph.D., who has been studying air hygiene at the institute since 1935, has been appointed to the fellowship.

### RHODE ISLAND

**Hospital Building Named for Dr. Adolf Meyer.**—A new psychiatric clinic building at the State Hospital for Mental Diseases, Howard, was dedicated October 18 and named in honor of Dr. Adolf Meyer, Henry Phipps professor of psychiatry, Johns Hopkins University School of Medicine, Baltimore. The semiannual meeting of the New England Society of Psychiatry was held in the afternoon following the dedication. Dr. Meyer and Dr. John E. Donley, Providence, made addresses at the dedication exercises. An appropriate plaque was installed in the lobby of the building and Dr. Seth F. H. Howes, superintendent of the hospital, presented to Dr. Meyer a scroll commemorating the occasion. In the afternoon Dr. Meyer addressed the psychiatric society on "The Psychiatric Hospital in a Progressive Health Program." In the evening a dinner was held in honor of Dr. Meyer at the University Club in Providence, under the auspices of the Rhode Island Society for Neurology and Psychiatry. Dr. Walter C. H. Weigner, Providence, president of the society, presided and Dr. Arthur H. Ruggles, Providence, state commissioner of mental diseases, was toastmaster. The speakers included Drs. Charles Macfie Campbell, Boston, Eugen Kahn, New Haven, and Dr. Meyer. The new building is part of a \$5,000,000 building program at the state hospital. It has a capacity of 120 beds and was built at a cost of \$296,500.

### TENNESSEE

**Society News.**—Drs. Edward E. Reisman Jr. and Earl R. Campbell addressed the Chattanooga and Hamilton County Medical Society, Chattanooga, October 13, on "Traumatic Injuries to the Extremities" and "Wrist Injuries" respectively. —At a meeting of the Hardin-Lawrence-Lewis-Perry-Wayne Counties Medical Society in Lawrenceburg recently the speakers were Drs. William E. Boyce, Flatwoods, on "The



Hydrogen Ion Concentration of the Blood"; Jack Witherspoon, Nashville, "Duodenal Ulcer"; Thomas J. Stockard, Lawrenceburg, "Poliomyelitis," and Oval N. Bryan, Nashville, "Use of Antipneumococcic Serum in the Treatment of Pneumonia."

**Personal.**—Dr. Leonard E. Ragsdale, at one time superintendent of the State Home for the Feeble-minded, Donelson, has been appointed superintendent of the Central State Hospital for the Insane, Nashville.—Dr. Malcolm T. Tipton, Union City, has been appointed a member of the state board of medical examiners to succeed Dr. Marcus G. Spingarn, Memphis, whose term expired.—Orren W. Hyman, Ph.D., dean of the University of Tennessee College of Medicine, Memphis, received the honorary degree of doctor of laws from Southwestern University, Georgetown, Texas, recently.

### VIRGINIA

**Changes in Health Officers.**—Dr. John G. McNeil, St. Charles, has been appointed health officer of the Montgomery County health district, succeeding Dr. William W. Fuller, Christiansburg, who is studying at the Johns Hopkins University School of Hygiene and Public Health. Dr. Willard W. Griggs, St. Charles, has succeeded Dr. George R. Carpenter in the Dickenson-Wise Counties district, and Dr. Eugene B. Shepherd, Chatham, has been made health officer of the Pittsylvania County district, succeeding Dr. Benjamin Randolph Allen. Dr. Carpenter and Dr. Allen are also at Johns Hopkins. Dr. Stephen J. Beeken, Lexington, recently assistant in the Rockbridge County district, has been appointed health officer of the Russell-Tazewell district with headquarters at Richlands. He succeeds Dr. Vernon A. Turner, Richlands, who is studying at the Harvard School of Public Health.

### WISCONSIN

**Society News.**—Dr. Karl C. Wold, St. Paul, addressed the Pierce-St. Croix County Medical Society, Baldwin, October 20, on "Common Disorders of the Eye: Their Diagnosis and Treatment."—Dr. Charles B. Puestow, Chicago, addressed the Winnebago County Medical Society, Oshkosh, October 6 on "Preoperative and Postoperative Care."

**Hospital News.**—St. Vincent Hospital, Green Bay, celebrated the fiftieth anniversary of its opening October 12-13 with a dinner for the staff, city and county officials and open house.—Milwaukee Hospital, Milwaukee, celebrated its seventy-fifth anniversary during the week of October 30; from a twenty bed institution it has grown to a capacity of 263.

**Personal.**—Dr. Glenford L. Bellis has retired as superintendent of the Muirdale Sanatorium and Blue Mound Preventorium, Wauwatosa. Physicians and employees of the sanatorium gave a testimonial banquet to Dr. Bellis October 13 and presented him with a plaque.—Dr. Albert J. Randall, assistant director of health in Kenosha, has been appointed director to succeed Dr. Gustave Windesheim, who retired October 15.

### GENERAL

**Massengill Firm Fined.**—Dr. Samuel E. Massengill, Bristol, Tenn., president of the S. E. Massengill Chemical Company, pleaded guilty in the federal court at Kansas City October 19 on sixty-two counts covering shipments of Elixir of Sulfanilamide-Massengill made from the Kansas City plant of the company. He was fined \$9,300. In federal court at Greenville, Tenn., October 3 the defendant's counsel pleaded guilty on 112 counts and was sentenced to pay a fine of \$150 for each count, making a total of \$16,800 (THE JOURNAL, October 22, p. 1567).

**Special Society Elections.**—Dr. Edward S. Godfrey Jr., New York state commissioner of health, Albany, was chosen president-elect of the American Public Health Association at the annual meeting in Kansas City, October 25-29, and Abel Wolman, Dr. Eng., Johns Hopkins University School of Hygiene and Public Health, Baltimore, was installed as president. The following were elected vice presidents: Drs. Albert Grant Fleming, Montreal, Canada; Leonides Andreu Almazan, chief, department of health, Mexico, and Edwin H. Schorer, Kansas City. The 1939 meeting will be in Pittsburgh.—Dr. Louis L. Williams Jr., U. S. Public Health Service, Washington, D. C., was chosen president-elect of the American Society of Tropical Medicine at the annual meeting in Oklahoma City November 15-18. Dr. Alfred C. Reed, San Francisco, became president; Drs. Sterling S. Cook, Portsmouth, Va., and E. Harold Hinman, Wilson Dam, Ala., were elected vice president and secretary respectively.—Dr. James K. McGregor, Hamilton, Ont., was chosen president-elect of the American Association for the Study of Goiter at the recent annual meeting

during the International Goiter Conference in Washington, D. C. Dr. Frank B. Dorsey Jr., Keokuk, Iowa, became president and Dr. Claude J. Hunt, Kansas City, was elected vice president. Dr. William Blair Mosser, Kane, Pa., is corresponding secretary and Dr. George C. Shivers, Colorado Springs, recording secretary.—Dr. Paul A. O'Leary, Rochester, Minn., was elected president of the American Academy of Dermatology and Syphilology at the annual meeting in St. Louis in November. Dr. Harther L. Keim, Detroit, was elected vice president and Dr. Earl D. Osborne, Buffalo, secretary. The 1939 meeting will be held in Philadelphia.

**Fellowships in Medical Sciences.**—The National Research Council announces that the following fellows, appointed by the medical fellowship board, have begun their work:

Dr. Louis K. Alpert, Chicago, at the Rockefeller Institute for Medical Research, New York.  
Philip P. Cohen, Ph.D., Madison, Wis., at the University of Sheffield, England.  
Thomas H. Davies, Ph.D., Baltimore, at the California Institute of Technology, Pasadena.  
Dr. Carl L. Larson, Butte, Mont., at the University of Rochester (N. Y.).  
Dr. Arthur P. Richardson, San Francisco, at John Hopkins University, Baltimore.  
Jane A. Russell, Ph.D., Berkeley, Calif., at Yale University, New Haven, Conn.  
Wilfred W. Westerfeld, Ph.D., St. Louis, at Oxford University, Oxford, England.

**Symposium on Mental Health.**—The section on medical sciences of the American Association for the Advancement of Science will conduct a symposium on mental health at the annual Christmas meeting in Richmond, Va., December 28-30. Sessions will be held at the Commonwealth Club except the final general session, which will be at the Mosque. Contributions to the symposium will be printed in advance and the sessions will be devoted to discussion of them. One topic will be discussed at each session. Dr. Charles Macfie Campbell, professor of psychiatry, Harvard University Medical School, Boston, will give the summary and address at the general session. Among the contributions listed in the program are:

Dr. Charles P. Fitzpatrick, Providence, R. I., Facilities for Research.  
E. Morton Jellinek, M.Ed., Worcester, Mass., Function of Biometric Methodology in Psychiatric Research.  
Dr. George Gilbert Smith, Boston, Relationship of Birth Control to Mental Conditions.  
Dr. John D. Reichard, Ellis Island, N. Y., Immigration and the Mental Health of Communities.  
Carney Landis, Ph.D., New York, and James Page, Ph.D., Rochester, N. Y., Magnitude of the Problem of Mental Disease.  
Dr. Helen Flanders Dunbar, New York, Bearing of Emotional Factors on Social-Health Programs Dealing with Economic Disability.  
Edward Sapir, Ph.D., New Haven, Conn., Psychiatric and Cultural Pitfalls in the Business of Getting a Living.  
Charles C. Limburg, Ph.D., Lexington, Ky., Community Differences and Mental Health.  
Dr. Winfred Overholser, Washington, D. C., Psychiatric Expert Testimony.  
Dr. George S. Stevenson, New York, Psychiatry in a Community.  
Dr. Edward A. Strecker, Philadelphia, Undergraduate Instruction in Psychiatry in the United States and Canada.

Dr. Thomas M. Rivers, New York, is chairman of the section on medical sciences and Malcolm H. Soule, Sc.D., Ann Arbor, Mich., is secretary. Dr. Walter L. Treadway of the U. S. Public Health Service, Lexington, Ky., is chairman of the program committee.

## Government Services

### Government Dedicates Narcotic Hospital at Fort Worth

The U. S. Public Health Service hospital for narcotic addicts at Fort Worth, Texas, the second of its type, was dedicated October 28. Dr. Thomas Parran, surgeon general, U. S. Public Health Service, made the dedicatory address and other speakers were Dr. Lawrence Kolb, assistant surgeon general in charge of the division of mental hygiene of the public health service, and James V. Bennett, director of the bureau of prisons of the department of justice. The new institution covers 1,400 acres and cost \$4,000,000. It includes an administration building, a clinical ward building, a maximum custody ward, residences for personnel and maintenance structures. A prolonged treatment building for advanced cases of addiction will be ready in 1939. The first narcotic hospital at Fort Worth unit places less emphasis on custodial features, such as high gates and walls and inclosed courts. Passed Assistant Surgeon William F. Ossenfort of the service, medical director of the new hospital, is a graduate of Washington University School of Medicine, St. Louis.

## Foreign Letters

### LONDON

(From Our Regular Correspondent)

Nov. 12, 1938.

#### Cardio-Omentopexy

The important advance of Mr. Laurence O'Shaughnessy in introducing the operation of cardio-omentopexy to provide collateral circulation in cases of cardiac ischemia, with its resultant angina pectoris, has been described in previous letters. The report of the Royal College of Surgeons for 1937-1938 contains a note on the experimental and clinical work performed by him during the year in conjunction with Dr. Slome, on which they have a paper in preparation. They have demonstrated that vascular continuity between a graft and the coronary tree can be obtained without the use of myocardial sutures, provided a special aleuronat preparation is used. Early experiences with the danger and difficulty of inserting stitches into a friable and degenerated myocardium make this an important technical advance. They have also shown that a graft applied to an adherent pericardium can still be effective. The importance of this observation was emphasized at a recent operation when they encountered pericardial adhesions at the site of a fairly recent infarct. Some of the experiments of Lezius, who first showed that the lung can rapidly form vascular adhesions with the heart after incision of the parietal pericardium, were repeated and his results confirmed.

The electrocardiogram of the grafted heart shows specific changes. Mr. O'Shaughnessy and Dr. Slome have records collected from several patients over a period of a year and more. An attempt to correlate their observations with electrocardiograms of grafted animals is still in progress. They have found that acute coronary occlusion may complicate the results of operation, and an experimental investigation of its treatment has become pressing.

The results in a series of twenty patients with cardiac ischemia operated on in the Lambeth cardiovascular clinic were published early in 1938. The survivors in this series and of more recent operations are still under observation. Patients who have survived the operation for one year and in some cases for two years continue to be active. One death from heart failure has occurred in the group, and if deaths from heart failure continue to be rare or absent as the group becomes larger, this fact alone will be significant.

#### Casualties of Air Raids

Speaking at the council dinner of the British Medical Association, the Right Hon. Walter Elliot, minister of health, said that on June 1 he took over the responsibility of organizing the emergency hospital system against the possibility of air raids. A survey had already been made of 3,000 hospitals and institutions and 400,000 beds. Hospital officers were appointed in every region of the country except London and asked to prepare schemes for the best utilization of hospital accommodation. At the same time a committee of medical experts presided over by Sir Charles Wilson, dean of St. Mary's Hospital, was appointed to consider the provision for London casualties, the type of hospital to be utilized for them and the extent to which peace time patients could be moved. In early August contact was established with every hospital throughout the country and they were asked to clear as many beds as possible on receiving warning from the government that an emergency had arisen. In September the international situation was so acute that plans had to be concentrated for immediate operation. Large orders were placed for hospital requirements, including surgical equipment for hospitals not then capable of dealing with casualties. On the last day of August every hospital officer was given instructions to accelerate plans

for clearing hospital beds, and 150,000 beds, with medical attendance and nursing complete, would have been available within twenty-four hours. That was only the beginning. Representatives of thirty-four of the larger London hospitals to be evacuated and representatives from the receiving areas were received by the ministry. Ambulances, both train and automobile, were organized. By September 24 the necessary number of stretchers were distributed to each hospital. From that moment the hospital evacuation scheme could have been put into operation within twenty-four hours of the warning. The crisis passed, but that was not the end of the possible emergencies. The hospitals were now being registered where surgical facilities could be improved.

### PARIS

(From Our Regular Correspondent)

Nov. 12, 1938.

#### Paris Physicians Protest Against Social Insurance

The abuse of free medical care by the public hospitals and dispensaries and the illegal extension of the original function of the social insurance authorities are arousing the French medical profession to make a vigorous campaign to put an end to a movement which renders it difficult for physicians to earn a living. In the notice sent out by the association of physicians in the department of the Seine, in which Paris is situated, for a meeting to be held Nov. 4, 1938, the following plea was made for a full attendance:

1. It is becoming more and more difficult, in fact almost impossible, to practice in Paris and the adjacent areas.
2. The public hospitals and dispensaries, which are not subjected to the excessively high taxes which physicians must pay, are doing all they can to give free medical attention without any inquiry as to the ability of the sick to pay. Such institutions should treat only indigents.
3. The social insurance organization was created to insure the worker earning up to a certain sum annually, now 30,000 francs, so that he might be able to pay for medical care. Instead of limiting their activities to this commendable objective, the social insurance authorities have begun to make serious inroads on the work of private practitioners by attempting to organize facilities for treating the insured worker. Every effort is being made to turn the insured from specialists and general practitioners by urging them to enter public hospitals or receive treatment at the many public dispensaries.
4. The situation has become so acute that the time has arrived for a more energetic campaign against these abuses, which make it impossible for a physician, after many years of preparation, to compete with the tendency toward state medicine.

#### Foreign Physicians Being Naturalized in France

Not only is there a marked increase in the number of first year medical students at all the medical schools here, but there is a fear that the government is giving permission to become naturalized to more physicians coming to France than there is room for in the profession. The number of foreign physicians who wish to practice here rose from four in 1935 to ninety-four in 1937. The Armbruster law, passed in 1933, requires all physicians of foreign birth not only to be naturalized but to serve the same length of time in the army or navy as those born in France or its colonies. At a recent meeting of the association which has charge of public relations for the French medical profession, the secretary, Dr. Cibrie, stated that permission to become naturalized is being too easily granted by the authorities, without adequate investigation of the past records of the applicants. An information bureau has been opened by the Confederation of Medical Syndicates, as the central organization is termed, to furnish the authorities with all data as to whether or not an applicant for naturalization is worthy of remaining in France.

### Antitoxin-Toxoid Treatment of Diphtheria and Tetanus

The question of whether the transitory passive immunity following the injection of diphtheria or tetanus antitoxin can be converted into a more permanent active immunity by simultaneous use of the diphtheria or tetanus toxoid has been the subject of papers at recent meetings of the Société médicale des hôpitaux of Paris. At the July 22 meeting the results of the combined use of the diphtheria antitoxin and the toxin were reported from three Paris hospitals. In the first paper Drs. René Martin and his co-workers stated that they had given the treatment to twelve children with diphtheria. A subcutaneous injection of 0.1 cc. of the toxoid was followed twenty minutes later by a single large dose of antitoxin. Forty-eight hours later a second injection, varying from 0.3 to 0.5 cc. of the toxoid, was given. Subsequently the toxoid in gradually increasing doses, beginning with 1 cc., was given every five days. Aside from slight febrile and local reactions after the first and second injections of the toxoid, no ill effects were noted. These reactions seem to be of an antigenic and not of an allergic character.

The titer of the antitoxin in the blood was measured at frequent intervals after the first injection of the toxoid. These determinations showed that the passive immunity conferred by the antitoxin does not interfere with the development by the toxoid of an active immunity in the majority of cases. Patients who had a well marked incipient immunity before the antitoxin was given showed a striking rise in the titer of the antitoxin in the blood after injection of the toxoid. Patients who failed to show any antidiphtheria immunity before being given the antitoxin showed a distinct but less marked increase in the titer of the antitoxin in the blood after injection of the toxoid. These observations appear to confirm the theory of Prof. Gaston Ramon that the brief transitory passive immunity conferred by the diphtheria antitoxin is succeeded by an active immunity which is more stable and of longer duration when the toxoid also is given.

#### OBSERVATIONS ON SOLDIERS

In a second paper, Drs. Solier and Jaulmes reported their observations on eleven soldiers with diphtheria at the large Val-de-Grace Hospital. A diphtheria toxoid with a titer of 150 units per cubic centimeter was used. A dose of 0.1 cc. was given the first day and was followed one hour later by a massive single dose of diphtheria antitoxin. This was followed by the injection at regular intervals during the remainder of the hospitalization of gradually increasing doses of the diphtheria toxoid. The eleven patients all recovered, no reaction of any importance following the use of the diphtheria toxoid being noted. Estimations of the titer of diphtheria antitoxin in the blood serum of the eleven patients were made over a period of six months. These estimations showed the constant presence of a titer of antitoxin in the blood serum adequate to protect the patient against a recurrence of the infection. This observation shows the advantage of the use of Ramon's combined antitoxin and toxoid administration as applied to a collectivity such as an army.

#### OBSERVATIONS ON CHILDREN

In a third paper, Drs. Darré and Lafaille reported their results with thirty-three children who had diphtheria. Of these, four had a malignant type, four had a severe form and sixteen had moderately severe form. In the last-named group, although some were not seen until the third or fourth day, no paralysis of the soft palate followed. In the seven with severe involvement, in spite of extensive formation of false membrane, no complications were noted. In all four with the malignant type an early paralysis of the soft palate was observed but there were no other sequels, such as generalized paralysis or cardiac and respiratory symptoms. These four children all recovered,

although in one the prognosis appeared very unfavorable. There were no deaths in the other twenty-nine cases.

The mode of administration in the thirty-three cases was as follows: On admission the child was given an injection in the left subscapular region of 0.1 cc. of a purified diphtheria toxoid with a titer of 150 units to the cubic centimeter. A half hour later a single massive dose of antitoxin, varying from 18,000 to 40,000 units according to the severity of the attack, was injected in the abdominal region. Forty-eight hours later, 0.5 cc. of the toxoid was injected, and then at intervals of five days two injections of toxoid, 1 cc. and 2 cc. respectively, were given. Before every injection the titer of antitoxin in the blood serum was determined, and it showed results which agreed with those of the observers cited.

In the discussion of these papers Dr. Marquetry failed to share the enthusiasm which the others had expressed regarding this new treatment of diphtheria. The number of patients thus far treated is too small to permit definite conclusions to be drawn. At present he believed that the antitoxin-toxoid treatment greatly complicated matters.

### Brucellosis Congress

The subject selected by the Federation of Medical Societies of Northern Africa for its next congress is brucellosis. The meeting will be held at Oran, Algeria, in April 1939. The titles of the papers to be read are epidemiology of the brucelloses, bacteriologic identification, clinical forms, medical and surgical complications, treatment, animal brucellosis and prophylaxis in Tunis, Algeria and Morocco. Those wishing to attend the congress are asked to write to Dr. René Solal, 16 Boulevard Joffre, Oran, Algeria.

### Many Physicians in French Parliament

There are a relatively large number of physicians in both the Chamber of Deputies and the Senate. At a recent election for senators in thirty departments, twelve physicians were elected or reelected. Many important laws affecting the medical profession have had their origin in bills submitted by physicians who were deputies or senators.

### Death of Proctologist

Many American proctologists have visited the clinics of Dr. Raoul Bensaude of Paris, who died during October. His book on rectosigmoidoscopy is used all over the world, and before his death he had just completed the fourth volume of a series on diseases of the intestine.

### BERLIN

(From Our Regular Correspondent)

Nov. 1, 1938.

### Genealogic Survey of the German People

A new comprehensive type of genealogic survey based on previous investigation has been ordered by the minister. This survey is basically intended to include the entire population, although it will at first concern itself with those groups among which eugenic and racial hygienic measures have been or are being carried on according to recognized legal stipulations. The new survey will represent in general an assembly of all data which may be relevant to the evaluation of the eugenic and racial status of familial groups and their members. Health officials record the data with regard to individual persons in a genealogic card catalogue and the data on familial groups in a special registry. The registration place for each person is the health bureau having jurisdiction over his place of birth. A table of the familial group has been devised which forms the matrix of a genealogic axis about which all particular data with regard to a group are assembled. Such a table is created for each family. The sum of familial data go to make up the registers of familial groups. The tables are to be compiled for as great a number of families as possible in order to promote the genealogic survey of the entire population.

### New Regulations for Nursing

The national government has just issued a "Statute for Regulation of Nursing," which contains certain innovations. In Germany, as elsewhere, a crisis in nursing has long existed. This crisis, according to a statement emanating from professional sources, expresses itself most clearly in a lack of a new generation of persons willing to enter Christian nursing orders. This state of affairs has been exacerbated by the spiritual degeneration incident to the Nazi revolution. The acute shortage of younger persons in the religious nursing organizations has been paralleled by a stronger influx into the Nazi Sisterhood as well as into the German Red Cross, the latter group having been reorganized along Nazi lines. Nevertheless, the need for a greater number of younger nurses is still urgent; the number of training schools is likewise inadequate. These circumstances underlie promulgation of the new decree, which now, for the first time, envisages a nationwide regulation of the nursing profession. Public hospitals are now compelled to establish and maintain nurses' training schools either at their own expense or, if necessity requires, with the aid of public funds. These schools must enroll the young apprentice sisters according to the maximal quotas prescribed by law for each institution. The training of male nurses is similarly regulated. The director of a nurses' training school must be a physician and the assistant director either a nursing sister or a male nurse. These officers must be morally and politically reliable (Nazi style) as well as of German blood. Like qualifications are demanded of matriculants in the nursing schools. Hereafter the course of training will cover only one and one-half years, instead of two years, as formerly. Professional training must be predominantly practical; the theoretical courses must be in part conducted by physicians. An official handbook serves as the basis of instruction. The curriculum must include an introduction to "weltanschaulichen," ethical principles of the nursing profession and, besides, regular classes in bodily hygiene. Compulsory insurance against personal injury and sickness is stipulated. Since October 1 only persons who hold special official licenses have been permitted to practice the nursing profession. The license is issued to a person who has passed the examination, but at first the nursing activities of the graduate are restricted to a public hospital. Only after a year of nursing in such an institution is the licensee certified for nursing outside a public hospital. A license may be revoked if the essential prerequisites of its granting become nullified, for example on the basis of political and moral unreliability, bodily or mental handicap or addiction to alcohol or narcotic drugs. Jews may practice nursing only among other Jews and in Jewish hospitals. Jewish nurses can receive training only in Jewish schools.

The new law represents a great improvement over the previous situation, in which the practice of the nursing profession was open to all and without government recognition.

### Psoriasis

Julius Mayr, professor of dermatology at Munich, has published a study of the problem of the heritability of psoriasis vulgaris. The author found analogous cases in a pair of enzymotic female twins. It is significant that the disease was manifested earlier and assumed a severer form in the twin whose bodily weight was the greater. From study of a family tree which comprised records of fifty-eight members over four generations, it was ascertained that psoriasis had been present in the generation of the grandparents but had reappeared only in the twins (four siblings of the latter were unaffected). The parent generation exhibited no signs of psoriasis. Also from the genealogic table it was ascertained that the penetrating power of psoriasis is often extremely slight, since the disease was found to be much less extensively distributed than would have been the case in a dominant hereditary transmission. It appears noteworthy that in this family diabetes was present in three members on the same (maternal) side.

### Prof. Karl Sudhoff Is Dead

Prof. Karl Sudhoff, former ordinarius of the history of medicine at Leipzig University, died shortly before completion of his eighty-fifth year. A country practitioner for some thirty years, Sudhoff in 1905 left the small town in which he had worked to accept appointment as extraordinarius in the newly founded chair of medical history at Leipzig. This chair was the first of its kind in Germany. Sudhoff's publications on medical history attracted widespread attention. While engaged in general practice, he had earned a notable reputation as a Paracelsus scholar. At Leipzig he grew to be the leading medical historian. His research on manuscripts represented surprisingly rich contributions to our knowledge of medieval medicine. In 1903, in collaboration with the chemist Kahlbaum, Sudhoff founded the German Society of Medical and Natural Scientific History. At Leipzig he established and headed the first regular Institute of Medical History. In the following decades Sudhoff's activities, and especially his writings, brought modern medicohistorical research into high regard. Worthy of note in addition to the mentioned paracelsian studies is Sudhoff's pioneer work in medieval balneology and the history of syphilis. The guiding principle of Sudhoff's thought was constantly to serve the present by study of the past. In 1919 he became ordinarius and his retirement took place in 1925. Later, after his successor, Prof. H. E. Sigerist, had quit Leipzig for Baltimore, Sudhoff resumed professorial activity and directorship of the institute. His eightieth birthday found him still vigorously active in this capacity. Sudhoff was greatly honored for his services. Among other things he was doctor honoris causa of philosophy and veterinary medicine and honorary member of the Royal Society of Medicine of London and of the Society of Medical History of Chicago. The German Society of Medical History changed its style to "Sudhoff-Gesellschaft" in his honor. Sudhoff was the extremely active editor of "Classics of Medicine," "Studies in Medical History" and the journal *Archiv für Geschichte der Medizin*, among other publications.

### NETHERLANDS

(From Our Regular Correspondent)

Oct. 8, 1938.

### The Institute of Thermology

The Warmte Stichting (institute of thermology) foundation has commemorated its tenth anniversary. This foundation, in addition to its usual function of inspection, has examined such problems as desiccation of grain, the ventilation of stables, the radiation of hearths and stoves, the conduction of heat in building materials and buildings, and central heating. New methods of measurement have been developed by the institute; among others a method for gaging the ventilation of dwelling rooms and work rooms, and a thermo-electric instrument for measurement of humidity. The foundation's chief of technical service took an active part in the work of the commission appointed to study atmospheric conditions in the buildings constructed by the Royal Institute of Engineers.

### Combined Immunization Against Scarlatina and Diphtheria

In North Holland province, since 1930, tens of thousands of children have submitted to combined immunization against scarlatina and diphtheria, effected by a mixture of diphtheria antitoxin and scarlatina antitoxin. This immunization has favorably influenced the incidence of diphtheria and also, to a lesser degree, the incidence of scarlatina. In 1937, among 25,018 inoculated children from 6 to 13 years of age, the scarlatina morbidity was 15.1:10,000; among 29,127 children not immunized the rate was 50.1:10,000. Inoculation did not cause any serious complications, although local reactions occurred sometimes accompanied by a scarlatiniform exanthem and slight elevation of temperature.

## JAPAN

(From Our Regular Correspondent)

Oct. 29, 1938.

## Air Raid Experiment in a Basement

For the protection of air raid refugees, the Industrial Hygiene Society, the planning board of the home office and the city protection association at Kanda joined September 12 in making a three hour experiment in the basement of the Hundredth Bank in the middle of Tokyo. Seventy adults participated, including forty-two examiners and inspectors. The directors were Shigeyuki Kitaura and Kentaro Kuroyanagi, engineers. The department of architecture and the sanitation department of the Tokyo Imperial University participated. The army and the navy sent its inspectors. The aim was to observe the ventilation when many refugees were shut up in a closed place and to learn how long they could remain. The basement was provided with every protection against poison gas, and every crevice was sealed up with gum tape. The twenty-eight examinees, of whom the oldest was 64 and the youngest 18, were all male. After a physical examination they went down into the basement. They wrote down on cards at any time they wanted what they felt and thought. The room was 25 square meters in area and 2.6 meters in height. As the examinees were closely packed in this room the temperature and humidity were reported every half hour to the office on the first floor. At 1:35 p. m. the temperature was 28.1 C. (82.5 F.) and the humidity 86, but they both gradually rose, and at 4:35 the former was 32.6 C. (90.7 F.) and the latter 99. At 4:18 a man of 48 found that he was unable to remain, while all the rest stood firm for the three hours without any notable ill effects. Further stay was thought to be dangerous. Detailed reports are to be made public in the near future.

## Military Medicine

Surgeon Major General Koizumi, chief of the bureau of military medicine, made a report on recent progress at a meeting of the Kyushu Medical Society. He defined military medicine in its broad sense as quite different from the military medicine based on fighting, or individual treatment. Medicine which aims to treat individuals has checked the progress and development of military medicine. In its broad sense military medicine requires public health establishments, social supplementary training and suitable surroundings for every profession and business. Universal strengthening of the nation's health ought to be considered. In the narrow sense, military medicine aims to strengthen the soldier's physical constitution. Medicine ought not to confine itself within its old circles but should dare to embrace researches into the social life. The speaker went on to the problem of how to have better efficiency in fighting, how to obtain a large quantity of pure water to supply soldiers, how to provide soldiers with ample food in the field and how to reeducate the wounded to furnish them with new occupations. He added that in the past war the number of the ill at the front was three or four to one wounded in fighting, but that in the present war the number has been reduced to 1.5 with illness to one wounded. This fact shows the development of military medicine.

## Reopening of Peking University

The old Peking University in North China was compelled to close because of the war between China and Japan. It is now making preparations for resuming lectures, and a great change in the organization is going to be realized with aid from Japan. The medical department, which was opened recently, has as its dean Prof. Dr. Hisomu Nagai, who had been dean in the Formosa Medical College after retirement from Tokyo Imperial University, and twelve professors and assistant professors, all Japanese, have been appointed. The agricultural department was opened in September with many Japanese professors. An engineering department will be attached to the

university, also with many Japanese on its staff. The total number of Japanese professors is estimated to be over sixty. The course is to be four years, and postgraduate courses will be founded to train graduates who wish to be specialists.

## All Medical Men Must Register

The government has enacted a new law for the registration of persons who are connected with medicine. The law requires reports from every physician, dentist, pharmacist and nurse who lives in Japan or in its territory abroad, including the South Sea islands. Once in every four years, on August 1, such persons are obliged to present a report concerning their ability to serve the government. Those who fail to make returns are liable to a penalty of 500 yen (\$135). Some of the chief articles in the report concern military service, condition of health, possibility of engaging in the national mobilization and family relations. About 59,700 physicians, 21,000 dentists, 26,700 chemists and 110,000 nurses are expected to make reports.

## Dr. Irisawa Is Dead

Dr. Tatsukichi Irisawa, honorary professor of Tokyo Imperial University, died at the age of 74 at the university hospital of pyelitis. After graduating in 1889 he was sent by the government to Germany to study for several years. In 1902 he was appointed to the chair of internal medicine. In 1921 he was made dean of the medical department and at the same time was appointed chief of court physicians. He held the latter position until 1927, when he resigned. In his will he asked his followers to dissect his body. He especially requested that his brain be dissected, for he had suffered from infantile paralysis at the age of 2.

## Marriages

MARTIN A. COMPTON, 1st Lieut., M. C., U. S. Army, Fort Benjamin Harrison, Ind., to Miss Bertha Mac La Fara of North Vernon, October 22.

DONALD T. HUGHSON, Madison, Conn., to Dr. FRANCES KATHRYN GRAMLING of Milwaukee, September 28.

WILLIAM C. SHEEIAN, Stevens Point, Wis., to Miss Antoinette M. Doolan of Madison, October 22.

MAURICE A. F. HARDGROVE, Milwaukee, to Miss Olive Van Susteren of Little Chute, Wis., September 3.

ARTHUR L. REINARDY, Stevens Point, Wis., to Miss Helen Steingraeber of Kewaunee, September 17.

JOHN P. HARNEY, Hartsdale, N. Y., to Miss Phyllis M. Hannemann of New York, August 6.

OTTO E. TOENHART, Sheboygan, Wis., to Miss Bessie McIntyre of Madison, September 17.

ALBERTI FRASER LAPSLEY, Badin, N. C., to Miss Mary Jane Hall of Roanoke, Va., November 12.

HOWARD J. LANEY, Prescott, Wis., to Miss Katherine V. May of Madison in September.

EUGENE E. BURZYNSKI, Laona, Wis., to Miss Helen Krieger of Milwaukee, September 30.

THOMAS PAINE SALTIEL, Chicago, to Miss Gene Sternberg of New York, November 14.

HAROLD L. MILLER to Miss Margaret Marian Plonsker, both of Milwaukee, August 10.

MYRON T. MCCORMACK to Miss Edna Lucille Purtell, both of Milwaukee, September 3.

CHARLES QUIRICO DE LUCA to Miss Cecilia McCarthy, both of Philadelphia, October 29.

LEO A. JORDAN to Miss Adrienne L. Bates, both of Saginaw, Mich., September 22.

HARVEY G. E. MALLOW to Miss Alice Dierker, both of Watertown, Wis., July 21.

HUGH A. CUNNINGHAM to Miss Mildred Owen, both of Milwaukee, August 28.

FRANK A. MAJKA to Miss Ruth N. Ryan, both of Pueblo, Colo., October 24.

WILLIAM F. RAGAN, Milwaukee, to Miss Myrtle Halverson, September 24.

## Deaths

**Addinell Hewson** • Philadelphia; Jefferson Medical College of Philadelphia, 1879; emeritus professor of anatomy, Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania; formerly professor of anatomy and histology at Temple University School of Medicine; at various times assistant professor of anatomy and demonstrator at his alma mater; fellow of the American College of Surgeons and member of the American Association of Anatomists; served on the staff of the Episcopal Hospital, where he was dispensary surgeon from 1887 to 1904; surgeon to St. Timothy's Hospital, now known as the Memorial Hospital, from 1894 to 1928; aged 83; died, October 27, at his home in Bryn Mawr, Pa.

**Leo Melville Crafts** • Minneapolis; Harvard University Medical School, Boston, 1890; an Affiliate Fellow of the American Medical Association; professor of nervous and mental diseases, Medical Department of Hamline University, 1893-1908, and dean, 1897-1903; past president of the Minnesota Neurological Society; served during the World War; delegate to the International Congress of Medicine, London, 1913, and the International Neurological Congress, Berne, Switzerland, 1931; on the staffs of the Minneapolis General, St. Mary's, St. Barnabas, Asbury, Swedish, Eitel and Maternity hospitals; aged 74; died, September 22, of coronary thrombosis.

**Frank Sidle Lynn** • Baltimore; University of Maryland School of Medicine, Baltimore, 1907; professor of clinical surgery at his alma mater; member of the American Surgical Association and the Southern Surgical Association; formerly vice president of the Medical and Chirurgical Faculty of Maryland; fellow of the American College of Surgeons; visiting surgeon to the University, Mercy, Franklin Square and Bon Secours hospitals, Hospital for Women of Maryland and Baltimore City Hospitals; aged 54; died, September 26, of cerebral hemorrhage.

**John Clement Heisler** • Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1887; since 1930 emeritus professor of anatomy at his alma mater and professor of anatomy, 1916-1930; professor of anatomy at the Medico-Chirurgical College of Philadelphia, 1898-1916; member of the American Association of Anatomists; author of "Textbook of Embryology," 1898, 1901 and 1907, and "Textbook of Practical Anatomy," 1912; aged 76; died, September 9, of chronic myocarditis.

**John Bruce McCreary**, Shippensburg, Pa.; University of Maryland School of Medicine, Baltimore, 1892; member of the Medical Society of the State of Pennsylvania; formerly deputy secretary of health for Pennsylvania and chief of the bureau of child health; served during the World War; past president of the American Association of School Physicians; on the staff of the Chambersburg (Pa.) Hospital; aged 68; died, September 13, of coronary embolism.

**John Martin Julius Raunick**, Harrisburg, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1900; member of the Medical Society of the State of Pennsylvania; health officer; past president of the Dauphin County Medical Society; past president of the Harrisburg Academy of Medicine; formerly on the staff of the Harrisburg Hospital; aged 63; died, September 15, of arteriosclerosis.

**William Woodburn** • Boone, Iowa; Hahnemann Medical College and Hospital, Chicago, 1888; past president and secretary of the Boone County Medical Society; health officer; president of the Iowa Public Health Association; on the staff of the Boone County Hospital; aged 78; died, September 2, of cerebral hemorrhage with right hemiplegia.

**Myers Worman Horner**, Mount Pleasant, Pa.; Jefferson Medical College of Philadelphia, 1896; past president and secretary of the Westmoreland County Medical Society; formerly deputy coroner; at one time member of the school board; on the staff of the Henry Clay Frick Memorial Hospital; aged 67; died, September 26, of multiple neuritis.

**Willard Henry Pierce**, Greenfield, Mass.; University of Vermont College of Medicine, Burlington, 1885; member of the Massachusetts Medical Society; formerly on the staff of the Franklin County Public Hospital; aged 72; died, September 24, in Montague of chronic myocarditis, empyema and bronchopneumonia.

**Frank Winfield Laidlaw** • Middletown, N. Y.; Jefferson Medical College of Philadelphia, 1903; district health officer; member of the consultant staffs of the Horton Memorial Hospital, Middletown, Monticello (N. Y.) Hospital and the Maimonides Hospital, Liberty; aged 62; died, September 20.

**Isaac N. McComb**, Brillion, Wis.; Chicago Medical College, 1877; member of the State Medical Society of Wisconsin; health officer in Brillion for many years and on numerous village and county boards; formerly member of the state legislature; aged 87; died, September 27, of arteriosclerosis.

**George Erastus Goodrich** • Phoenix, Ariz.; Rush Medical College, Chicago, 1906; fellow of the American College of Surgeons; on the staffs of St. Joseph's and Good Samaritan hospitals; surgeon to St. Luke's Hospital; aged 59; died, September 3, in Los Angeles of heart disease.

**Lawrence Ewald Lepper** • Los Angeles; University of California Medical Department, San Francisco, 1912; fellow of the American College of Surgeons; served during the World War; on the staff of the California Hospital; aged 51; died, September 18, of heart disease.

**Albert George Gorczyca** • Elizabeth, N. J.; Georgetown University School of Medicine, Washington, D. C., 1929; aged 32; on the staffs of the Alexian Brothers Hospital and St. Elizabeth Hospital, where he died, September 24, of hypertrophic cirrhosis of the liver.

**Frank Robert Smith Sr.**, Baltimore; University of Maryland School of Medicine, Baltimore, 1891; member of the Medical and Chirurgical Faculty of Maryland; formerly associate of medicine, Johns Hopkins University; aged 82; died, September 26, of heart disease.

**Raynauld Dobson Richman** • Hartford, Conn.; University of Buffalo School of Medicine, 1908; served in the World War; for many years connected with the Aetna Life Insurance Company; aged 53; died, September 16, of hypertensive cardiovascular renal disease.

**Kennard J. French**, Factoryville, Pa.; Kentucky School of Medicine, Louisville, 1905; member of the Medical Society of the State of Pennsylvania; aged 75; died, September 26, in the Moses Taylor Hospital, Scranton, of arteriosclerosis and hypostatic pneumonia.

**Robert Alexander Simpson**, Washington, Ga.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1884; member of the Medical Association of Georgia; aged 79; died, September 24, of carcinoma of the prostate.

**Elmer Hinckley Heath** • Buffalo; Harvard University Medical School, Boston, 1923; assistant dean and associate professor of medicine, University of Buffalo School of Medicine; aged 43; died, September 23, of hypertension and arteriosclerosis.

**Benjamin M. Watkins** • Derry, Pa.; Jefferson Medical College of Philadelphia, 1909; bank president; aged 54; on the staff of the Latrobe (Pa.) Hospital, where he died, September 30, of pulmonary embolism following injuries received in a fall.

**Cloud M. Jackson**, Elizabethtown, Ind.; Hospital College of Medicine, Louisville, 1903; member of the Indiana State Medical Association; served during the World War; formerly county coroner; aged 61; died, September 29, of myocarditis.

**Robert Lee Frisbie** • Rhinelander, Wis.; Marion-Sims College of Medicine, St. Louis, 1894; for many years deputy state health officer; aged 68; died, September 17, in the Wisconsin General Hospital, Madison, of cerebral arteriosclerosis.

**Ray H. Johnson** • Buffalo; University of Buffalo School of Medicine, 1893; fellow of the American College of Surgeons; aged 70; on the staff of the Deaconess Hospital, where he died, September 17, of fracture of the skull resulting from a fall.

**James Aubrey Lippincott**, Nice, France; Jefferson Medical College of Philadelphia, 1873; member of the Medical Society of the State of Pennsylvania and the American Ophthalmological Society; aged 91; died, September 23.

**Frank George Ungerman** • McKeesport, Pa.; University of Louisville (Ky.) Medical Department, 1912; aged 50; on the staff of the McKeesport Hospital, where he died, September 26, of cerebral hemorrhage and chronic nephritis.

**John W. Bachelor**, Oxford, Mich.; Detroit College of Medicine, 1897; member of the Michigan State Medical Society; served during the World War; aged 63; died, September 23, of carcinoma of the stomach with metastasis.

**John Warren Germany**, Ennis, Texas; Kentucky School of Medicine, Louisville, 1890; served during the World War; formerly on the staff of the Municipal Hospital; aged 71; died, September 23, of coronary thrombosis.

**Joseph Welch Scott**, West Point, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1887; member of the State Medical Association of Texas; aged 74; died, September 11, at the Ivy Hospital.

**Robert Burtis Blanchard** • Jamestown, N. Y.; University of Buffalo School of Medicine, 1906; aged 55; on the staff of the



Jamestown General Hospital and the Woman's Christian Association Hospital, where he died, September 15.

**Frank Mansfield Sharpe**, Oconomowoc, Wis.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1887; aged 75; died, September 13, of chronic myocarditis and arteriosclerosis.

**Samuel Beecher Pray** ♂ New Rochelle, N. Y.; University and Bellevue Hospital Medical College, New York, 1901; on the staff of the New Rochelle Hospital; aged 65; died, September 7, in the Glens Falls (N. Y.) Hospital.

**William Walter Pretts** ♂ Milwaukee; Northwestern University Medical School, Chicago, 1900; served during the World War; on the staff of the Veterans Administration Facility; aged 65; died, September 7, of heart disease.

**Alfred Elias Orr**, Montreal, Que., Canada; McGill University Faculty of Medicine, Montreal, 1888; at one time lecturer in anatomy and demonstrator of biology at his alma mater; aged 77; died, September 23.

**John Bernhard Thompson**, Wittenberg, Wis.; Milwaukee Medical College, 1912; served during the World War; aged 51; died, September 6, in the Memorial Hospital, Antigo, of peritonitis and ruptured gallbladder.

**Arthur Franklin Gerberich**, Limeport, Pa.; Medical-Chirurgical College of Philadelphia, 1909; member of the Medical Society of the State of Pennsylvania; aged 52; died, September 21, of pulmonary carcinoma.

**Aloys Heinen**, Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; aged 76; died in September in Germany of chronic myocarditis and arteriosclerosis.

**James W. Ludden**, Cincinnati; University of the South Medical Department, Sewanee, Tenn., 1894; aged 75; died, September 28, in St. Agnes Hospital, Philadelphia, of hypostatic pneumonia and arteriosclerosis.

**Thomas Richmond**, Guthriesville, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1881; member of the Medical Society of the State of Pennsylvania; aged 81; died, September 2, of uremia.

**Peter Lorentz Vistauet**, Thief River Falls, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1902; aged 67; died, September 22, of bronchopneumonia and myocardial insufficiency.

**Jacob B. Oliver**, Brazil, Ind. (licensed in Indiana in 1897); formerly a medical missionary and minister; aged 91; died, September 21, of carcinoma of the right cheek and jaw and bronchopneumonia.

**Philip Arlis Hilton**, Waynesboro, Va.; Howard University College of Medicine, Washington, D. C., 1920; aged 49; died, September 25, in the University Hospital, Charlottesville, of bronchopneumonia.

**Willard Hanks Gage**, Seattle; Eclectic Medical Institute, Cincinnati, 1899; aged 60; died, September 16, of injuries received in an automobile accident in the mountains near Jackson, N. Y.

**Harry Melville Dougherty** ♂ Pittsburgh; University of Pittsburgh School of Medicine, 1925; served during the World War; aged 41; died, September 13, of pulmonary tuberculosis.

**John Walton Shultz**, Kansas City, Mo.; University Medical College of Kansas City, Mo., 1902; aged 79; died, September 16, of chronic myocarditis, cystitis and arteriosclerotic nephritis.

**John Peyton Foster**, La Crosse, Mo.; Marion-Sims College of Medicine, St. Louis, 1893; aged 74; died, September 29, of acute dilatation of the heart, arteriosclerosis and nephritis.

**J. M. Caldwell**, Augusta, Ga.; Medical College of Georgia, Augusta, 1897; at one time demonstrator and instructor of obstetrics at his alma mater; aged 68; died, September 16.

**Adolph F. Wohlenberg**, Kooskia, Idaho; College of Physicians and Surgeons of Chicago, 1894; formerly a druggist; aged 76; died, September 23, of carcinoma of the prostate.

**Alexander Joseph Slaven**, Columbus, Ohio; Bellevue Hospital Medical College, New York, 1898; aged 67; died, September 19, of cerebral embolism and arteriosclerosis.

**Charles Terbush Haines**, Utica, N. Y.; Pulte Medical College, Cincinnati, 1887; on the staff of the Utica Memorial Hospital; aged 75; died, September 30, of heart disease.

**Robert C. Wear**, Baxter Springs, Kan.; University of Kansas City Medical Department, 1885; member of the Kansas Medical Society; aged 80; died, September 9.

**Lawrence Arthur Petty**, Charleston, W. Va.; University of Cincinnati College of Medicine, 1913; served during the World War; aged 52; died, September 14.

**Benjamin Frank Hutchings**, Crawfordsville, Ind.; Medical College of Ohio, Cincinnati, 1872; aged 92; died, September 29, of chronic nephritis and arteriosclerosis.

**Bruce Jonas Crisman**, Utica, N. Y.; Syracuse University College of Medicine, 1907; aged 56; died, September 29, in St. Luke's Hospital of heart disease.

**Rufus V. Gamble**, Elyria, Ohio; Western Reserve University Medical Department, Cleveland, 1871; aged 90; died, September 28, of intestinal obstruction.

**George Washington Henderson**, Westerville, Ohio; Starling Medical College, Columbus, 1892; aged 81; died, September 23, of cerebral hemorrhage.

**Johnston Frank**, Dallas, Texas; Medical College of Ohio, Cincinnati, 1880; Jefferson Medical College of Philadelphia, 1886; aged 81; died, September 29.

**Clarence Woodson Warnock**, Huntington, W. Va.; Kentucky School of Medicine, Louisville, 1907; aged 57; died, September 16, in St. Mary's Hospital.

**Mary Elizabeth Fetzer Mazza**, East Cleveland, Ohio; Western Reserve University School of Medicine, Cleveland, 1928; aged 36; died, September 14.

**Samuel Cooke Ingraham**, Philadelphia; Jefferson Medical College of Philadelphia, 1886; aged 88; died, September 11, of cystitis, prostatitis and uremia.

**Francis Boyd Carleton**, Boston; Boston University School of Medicine, 1894; aged 73; died, September 7, at his summer home in Sebago Lake, Maine.

**John C. Swatzlander**, Fontana, Calif.; University Medical College of Kansas City, Mo., 1897; aged 66; died, September 11, of cirrhosis of the liver.

**Napoleon B. Winfrey**, Kansas City, Mo.; Kansas City Medical College, 1881; aged 86; died, September 10, of chronic myocarditis and nephritis.

**C. E. Smith**, Enid, Okla.; Louisville (Ky.) Medical College, 1893; aged 72; died, September 10, in a local hospital of prostatitis and urinary calculi.

**Walter Kenney Barrett**, Milford, Del.; University of Pennsylvania Department of Medicine, Philadelphia, 1895; aged 68; died, September 10.

**Ward Greene Clarke**, Chicago; Rush Medical College, Chicago, 1882; aged 79; died, October 27, of coronary and cerebral thrombosis.

**Sara May Donnell Wolverton**, Merchantville, N. J.; Woman's Medical College of Pennsylvania, Philadelphia, 1904; died, September 27.

**John Francis Heffernan** ♂ Albany, N. Y.; Albany Medical College, 1901; on the staff of St. Peter's Hospital; aged 61; died, September 8.

**Walter Davis Wilson**, Schlater, Miss.; University of Tennessee Medical Department, Nashville, 1893; aged 71; died, September 23.

**Henry Franklin Bean**, Portsmouth, Ohio; University of Louisville (Ky.) Medical Department, 1876; aged 85; died, September 11.

**Charles Garfield Chapin**, Brantford, Ont., Canada; University of Toronto Faculty of Medicine, 1906; aged 54; died, September 26.

**Joseph Napoleon Bonaparte Rawle**, Brooklyn; Eclectic Medical College of the City of New York, 1899; aged 72; died, September 30.

**Andrew J. Allen**, Subiaco, Ark.; Gate City Medical College, Dallas, Texas, 1907; aged 70; died, September 20, of pulmonary tuberculosis.

**William Lynn Wilson**, St. Joseph, Mich.; Detroit College of Medicine, 1890; aged 71; died, September 6, of carcinoma of the prostate.

**Adam Hume Millar**, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1908; aged 58; died, September 28.

**Daniel Paul Odom**, Lyons, Ga.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1901; aged 68; died, September 25.

**Samuel McLean Withers**, Moultrie, Ga.; North Carolina Medical College, Davidson, 1902; aged 61; died, September 4.

**Hugh C. Cunningham**, Roganville, Texas; Jefferson Medical College of Philadelphia, 1885; aged 76; died in September.

**William A. Reed**, New York; Hahnemann Medical College and Hospital, Chicago, 1880; aged 83; died, September 15.

**Waldemar Ude**, St. Louis; Marion-Sims College of Medicine, St. Louis, 1892; aged 67; died, September 17.

## Bureau of Investigation

### TUCKER'S SPECIFIC FOR ASTHMA CRIES HELP!

#### New Legislation Causes Pain and Anguish to Proprietors of an Old, Old Asthma Specific

As long ago as May 20, 1911, the Bureau of Investigation (then known as the Propaganda Department of the American Medical Association) first called attention to the nostrum "Dr. Nathan Tucker's Specific for Asthma, Hay Fever and Nasal Catarrh." In a Notice of Judgment issued Sept. 29, 1911, the government declared the "specific" misbranded on two counts. Thirteen years later THE JOURNAL (Nov. 1, 1924) pointed out editorially that the Commissioner of Internal Revenue had replied to an inquiry from THE JOURNAL that, while "Tucker's Asthma Specific" carried a label admitting the presence of 5 grains of cocaine to the fluidounce, before the remedy reached the public the cocaine became hydrolyzed and there was either no cocaine or but an infinitesimal quantity. The commissioner also expressed the opinion that the mail-order distribution of this nostrum served "a great humanitarian cause"; therefore it had been decided by the Treasury Department to take no action enjoining its distribution. THE JOURNAL concluded its comments, in part, as follows:

"If it contains cocaine or a derivative of cocaine, and the Treasury Department has admitted that it does, then its sale violates the Harrison Narcotic Law, for that law applies just as much to the derivatives of cocaine as it does to cocaine itself."

The present promoters of the product appear to be Drs. W. B. and G. B. Robinson, and they are apparently concerned over the effect of the new Food, Drug and Cosmetic Act on their product. According to the Mount Gilead (Ohio) *Sentinel* for Sept. 8, 1938, Dr. W. B. Robinson addressed the local Kiwanis Club in part as follows:

"There are now patients using this remedy in every town of 500 or more population in the entire country, and this has resulted solely from one person securing relief and then telling others."

"Legislation has been recently passed at Washington which will force every such patient to come to Mount Gilead for treatment. [It would indeed be a sight worth seeing if citizens from every town of the United States of more than 500 population were to gather together into a Coxey's army and march on to Mount Gilead.—Ed.] Only a small percentage of such cases can afford to come to Mount Gilead, and as a result of this hasty and ill considered legislation thousands of asthma sufferers will be unable to secure relief."

"Unless an amendment is made to the law, thousands of asthma sufferers who now obtain relief from the use of this remedy will be doomed to suffer indefinitely, many of them all the remainder of their lives, because of their inability to come to Mount Gilead from their homes hundreds of miles away."

This colossal assertion by Dr. Robinson presumes that these sufferers could not obtain more scientific and efficacious treatment by inquiring of their family doctor, or an allergist in their locality, than they obtain at the present time from Mount Gilead.

The Drs. Robinson are so concerned about this matter that a form letter addressed "To Our Patients" is apparently being distributed at the present time. The letter says in part:

"The new law quite properly exempts physicians from its requirements, but into the final draft some influence slipped twenty-one words which provide that diagnosis may be made only after a personal examination."

The letter even goes so far as to admit that, "in treating most of the ills that flesh is heir to, a personal examination is essential [It adds, however] but 48 years of experience, and the statements in our text books have convinced us that this is an unnecessary and an unreasonable requirement when dealing with such characteristic syndromes as Asthma and Hay Fever."

It might be suggested that the Robinsons consult some more recent textbooks for details of skin tests, elimination diets and other means of determining the causative agents in asthmatic conditions. As a result of such tests, causative agents can be frequently eliminated and desensitization to such agents sometimes accomplished. But, of course, this constitutes scientific treatment.

The Drs. Robinson say that they are "delighted to see the continuing procession of patients that come to our office, but

experience has doubtless proven that we can relieve your Asthma or Hay Fever without the necessity of a personal examination." Why the "doubtless"?

The concluding paragraph of the form letter is especially interesting. It reads:

"At the next session of Congress we are going to ask for an amendment that will enable us to serve you as we have in the past. If you with our tens and tens of thousands of other patients will bring this to the attention of your Senators and Representative, either by a letter or a personal interview, we are sure our amendment will be accepted. We would appreciate copies of any letters, or report of your personal interview."

A parallel to this form letter was forwarded by Dr. W. B. Robinson "To Our Patients In New York" under date of Feb. 18, 1913. It read as follows:

"The Walker Bill No. 692 has been submitted to the Legislature of New York State. If this Bill becomes a law we cannot send you further fluid."

"If your physician should be fortunate enough to know a prescription that would relieve your asthma he could come to your bedside and give it to you. If, however, it contained cocaine you would render yourself liable to fine and imprisonment if you kept his medicine in your house over ten days; in other words, it would be unlawful for you to have in your possession over ten days any medicine which contained cocaine in any form or in any dosage. This means that if it happened to be eleven days after you received the prescription before you had an attack of asthma, you could not legally use it."

"The purpose of this law is to prevent the indiscriminate sale of cocaine to the drug fiends or in any way that might make drug users. In so far as it accomplishes this it is good. The workings of it, however, we are sure would be a very great hardship to you."

"We trust you will take this up with your Senators and Representatives, or with any prominent people you know in your State; give them your opinion of our Treatment; state to them frankly whether it has relieved you and if it has in any way produced a drug habit."

"If you know any of the Senators or Representatives personally, I would be pleased if you would give me a letter of introduction to them. "PLEASE ACT IMMEDIATELY."

It is interesting to note the more recent attempt on the part of this nostrum manufacturer to counteract the useful and effective measures which are part of the new Food, Drug and Cosmetic Act. The provisions which make up the new Food, Drug and Cosmetic Act are designed in part to prevent the mulcting of innocent people who believe that they can be treated by "long distance" for conditions which require personal medical attention.

### KELPEP, PROSTAX AND GLANMEND

#### The Frauds of Lord & Company Are Debarred from the Mails

One Mrs. Rose Lord Pressner of Ridgewood, Brooklyn, N. Y., doing business under the trade styles "R. Lord," "Lord & Co." and "Lord's," sold mail-order nostrums for the alleged cure of lost sexual vitality and allied conditions. From the evidence it appears that Mrs. Pressner contacted her victims through advertisements carried in newspapers which are not particular about the type of advertising they accept. She also, it is stated, purchased "sucker lists" from concerns that deal in such merchandise.

In her advertising Mrs. Pressner stated that she had "seen a lot of men worn down Physically and Mentally." She suggested that those who lacked the "power of erection" should take her "Kelpep," which, she claimed, was "number one in building up" and "one single teaspoonful [of which] contains more natural iodine than 427 pounds of spinach" and was "proportionately 700 times richer than oysters." She also recommended her "Glanmend," which she called "the newer tonic tablet treatment" that would "put brand new pep into your tired body almost like magic."

Mrs. Pressner was also solicitous of those who had symptoms of prostate "trouble." She declared that "a man is as old as his prostate." For these she had some rectal suppositories called "Prostax." In addition, as a sideline she added to her armamentarium for those males who lacked vim, vigor and vitality a device that she called "Giant Developer." This was actually a mechanical masturbator of a type that the Post Office has time and again debarred from the mails.

When Lord & Co., et al., were called on last April to show cause why a fraud order should not be issued against them, no person appeared at the hearing but a firm of attorneys forwarded a written answer and certain exhibits. The postal officials

declared that there were no physicians, chemists or pharmacists connected with the business but that Mrs. Pressner was the sole owner and the only person involved in the operation of the business.

Government chemists reported that Kelpep tablets consisted essentially of seaweed with a fraction over one one-hundredth of a grain of iodine to each tablet. The Glanmend "tonic" was found to contain some animal tissue with strychnine and saw palmetto. The strychnine was the only ingredient with a known pharmacologic effect, and the claim that Glanmend would restore sexual vitality was declared fraudulent. The suppositories which were supposed to cure "prostate trouble" were found to have a base of cocoa butter in which were incorporated about 3 per cent ichthammol and small amounts of atropine, hydrastine and oil of juniper. The claim that this would reduce the size of a hypertrophied prostate or eliminate all symptoms of prostate trouble was declared false.

Mrs. Pressner's scheme was declared to be one for obtaining money through the mails by means of false and fraudulent pretenses, representations and promises. The mails were closed to R. Lord, Lord & Co. and Lord's on July 1, 1938.

## Correspondence

### RACIAL DIFFERENCES IN HYPERTENSIVE DISEASE

To the Editor:—In THE JOURNAL October 29, page 1684, a reply to a query asking about the racial incidence of hypertension stated that there is no well defined racial difference in the incidence of hypertensive disease. This statement is not at all in agreement with the literature, especially that which has to do with hypertension in colored people.

The proneness of Negroes to hypertension and its resultant or concomitant cardiac and renal changes has been noted and studied by several investigators. Adams (*Am. J. M. Sc.* 184:342 [Sept.] 1932) made several blood pressure readings on each of 5,074 male employees and one reading on each of 9,000 applicants for employment. About one third of these were colored and the remainder white. The average white systolic pressure was 121 mm. and the diastolic 81 mm.; for the colored, systolic 128 mm., diastolic 85 mm. In each age group the Negro systolic pressures were from 4 to 13 mm. higher than those of the white men, and the diastolic pressures were from 2 to 6 mm. higher. Beyond 40 years of age the pressures of the Negroes advanced more rapidly than of the white men. The maximum differences of the average systolic pressures in the age groups occurred at ages 46-50 years and at 56-60 years, when the colored systolic pressures were respectively 11 mm. and 13 mm. higher. The maximum difference in diastolic pressure was in the 41-45 year and 56-60 year groups, which in both instances amounted to 6 mm. over the white. The average of the maximum systolic pressures of all 5 year age groups from 18 to 65 was 205 mm. for the white men and 222 mm. for the Negroes. The average of the minimum systolic pressures was 79 mm. for both races. Damage to the aortic valve in hypertension, as evidenced by an increased pulse pressure, occurs earlier and more frequently in Negroes. Jaffé (*Zentralbl. f. allg. Path. u. path. Anat.* 55:209, 1922) found, in his necropsy experience at the Cook County Hospital in Chicago, that hypertension and malignant nephrosclerosis were much more prevalent in Negroes and that also the average age at death was lower. Moritz and Oldt (*Am. J. Path.* 13:679 [Sept.] 1937) made a detailed study of arteriolar sclerosis in a necropsy population of 1,177 individuals. Negroes made up 20 per cent of this population but furnished 30 per cent of the cases of chronic hypertension, indicating again that the disease has a higher incidence among them than among the white men. Analysis of the ages in the hypertensive cases showed that the mean age

of the Negroes was eight years lower than that of the white men. These patients with hypertension died of uremia, cardiac failure or cerebral hemorrhage, but about the same percentage of Negroes and white men died of each of these causes. Histologic studies of each type, distribution and severity of arteriolar changes in white and colored nonhypertensive and hypertensive men showed no racial differences.

Schulze and Schwab (*Am. Heart J.* 11:66 [Jan.] 1936) applied the various theories that have been applied to explain hypertension to account for the difference between white persons and Negroes. They disclaim the role of inheritance, since hypertension is absent in native Africans and there is not enough intermixture with white persons to account for the departure from this African characteristic. Moreover, they say, the mendelian law of inheritance is not in accord with the excess of hypertension in Negroes over white persons, which amounts to 2.5 times. The effect of the change from African to American climate is considered but, although Europeans and Americans show a lowering of blood pressure in the tropics, there is no evidence that the contrary circumstances produce opposite results. Although syphilis is present in Negroes, its role in hypertension is questionable. (The relation of syphilis to hypertension is discussed by Horine and Weiss: *Am. Heart J.* 6:121 [Oct.] 1930.) Likewise diet and obesity are unsuitable as explanations of hypertension. Schulze and Schwab resort to the theory of nervous factors to account for the high rate of hypertension in Negroes. They believe that the true explanation is the stress and strain incident to adjustment to a new civilization.

Statistics show that arteriosclerosis causes relatively more heart disease and hypertension causes relatively less heart disease in white persons than in Negroes. Stone and Vanzant (*THE JOURNAL*, Oct. 29, 1927, p. 1473) found that 50.5 per cent of the heart disease in Negroes was caused by hypertension as compared to 45.3 per cent in white persons. Arteriosclerosis produced 19.8 per cent of the cases in white persons and 6.3 per cent in Negroes. In the same clinic a few years later Schwab and Schulze found that 42.4 per cent of the cases in white persons and 63.2 per cent of the cases in Negroes were due to hypertension and 35.9 per cent of the cases in white persons and 13.7 per cent of the cases in Negroes were produced by arteriosclerosis. Arteriosclerosis is a disease primarily of advanced age, and the lower rate of this condition in Negroes might mean a lower proportion of the upper age groups in this race.

Hedley (*Pub. Health Rep.* 50:1127 [Aug. 23] 1935) points out that Negroes dying in the arteriosclerotic-hypertensive group of heart disease do so at an earlier age than white persons. In his series the average age of Negroes at death was 54.6 years and the average age of white persons was 66.6 years. The peak of deaths of Negroes was at 40-49 years and of white persons it was 60-69 years. In the white persons 40.4 per cent of these deaths occurred at the age of 70 years or more but only 16.7 per cent occurred at this time among the Negroes. Death occurred before 40 years in 0.6 per cent of the white persons and in 12.9 per cent of the Negroes.

Jaffé was of the opinion that the large amount of hypertension in Chicago Negroes was due to their recent immigration from the South.

Polak (*Am. J. Obst. & Gynec.* 4:227 [Sept.] 1922) says that fibroids, which are very prevalent in Negro women, have no effect on blood pressure, although a relation between these two conditions has been suggested.

Schwab (*Proc. Soc. Exper. Biol. & Med.* 32:583 [Jan.] 1935) determined the results of the vasomotor test of Hines and Brown (*Ann. Int. Med.* 7:209 [Aug.] 1933) on 172 white persons and 153 Negroes between the ages of 15 and 35 years. In this test the hand and wrist were put in cold water (from 4 to 5 C., or 39 to 41 F.) and while in the bath blood pressure readings

were taken thirty, ninety and 150 seconds after immersion. He found that the elevation of blood pressure is more marked in Negroes and concluded that there is a quantitative racial difference in reaction to a standard vasomotor stimulus, indicating a more sensitive vasomotor mechanism in the Negro. This evidence is used in support of the neurogenic theory of hypertension.

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## Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

### AIR CONDITIONING FOR PNEUMONIA

*To the Editor:*—What is the latest method of treating both lobar and bronchial pneumonia in an air conditioned room in a hospital? What are the advantages? What are the contraindications?

ALBERT C. LUNDGREN, M.D., Minneapolis.

**ANSWER.**—Whenever a patient is placed in an oxygen tent, the atmosphere surrounding him is conditioned. When tents are well designed and operated, the atmospheric conditions assist cooling and maintain a desired partial pressure of oxygen and of carbon dioxide.

The essential factors in proper atmosphere conditioning have been analyzed and desirable conditions formulated (Bullowa, J. G. M.: *Management of the Pneumonias*, New York, Oxford University Press, 1937). The factors controlled are temperature, relative humidity, rate of air movement, oxygen concentration, carbon dioxide concentration and removal of noxious substances, either chemical or particulate, which cause odors.

The necessary loss of oxygen and the introduction of surrounding unconditioned atmosphere when services are rendered to the patient are inherent disadvantages in even well designed and operated individual oxygen enclosures or tents. Some patients have a feeling of confinement and isolation. Either the nursing and examinations are neglected in order to retain the high and uniform oxygen concentration or desirable and even essential atmospheric conditions are sacrificed.

In some climates and under some atmospheric conditions and, in the case of less severely stricken patients, uniform high oxygen concentration may be sacrificed in order that better nursing care may be provided and physical examinations performed. Nevertheless, in some late and prostrated patients disaster may follow when, for even brief periods, oxygen concentration is diminished to provide nursing care and careful physical scrutiny.

To overcome these disadvantages, oxygen rooms have been provided in some well equipped hospitals. In them patient and nurse are simultaneously enclosed. Both nursing care and the physician's observations may be provided without loss of optimal atmospheric conditions.

Conditions desirable for febrile anoxic patients may not be agreeable to those entering a well conditioned room from warm or humid surroundings. This may lead to unwise criticism. Recording instruments are accordingly desirable to proper operation of atmosphere control rooms.

Excellent, satisfactory air conditioned rooms are in use at the Rockefeller Institute, the Presbyterian and the Harlem hospitals in New York. Those responsible for the care of patients with lobar and bronchopneumonia in these hospitals believe that they are of great value and do not wish to give them up. In various centers improperly designed chambers have been built without suitable locks, adequate provision for air conditioning or economical maintenance of the oxygen concentration. Naturally, these have proved unsatisfactory and have been abandoned. The principle of air conditioning in the treatment of pneumonias is sound and in practice desirable and may be economical.

The cost of maintaining a well designed, maintained and operated oxygen chamber is not considerably greater than the cost of maintaining an oxygen tent. The first cost of installation is offset in the case of patients desperately ill by the much more satisfactory results.

### ESOPHAGOBRONCHIAL FISTULA

*To the Editor:*—A man aged 32 has had an esophageal-bronchial fistula for several years following a traction diverticulum. There is no evidence of tuberculosis. He has no fever. The blood sedimentation (Westergreen) is 30, the leukocytes number 10,100, and the hemoglobin (Sahli) is 100 per cent. He has had several attacks of bronchial pneumonia and complaints of violent coughing. X-ray examination shows esophageal-bronchial fistula of a large size and signs of gastritis and cardiospasm. He has been nourished through a duodenal sound with relief. He weighs 79 Kg. What treatment can be followed? Is there any chance of operating without opening the thorax?

L. ZWILLINGER, M.D., Prostějov, Czechoslovakia.

**ANSWER.**—Nonmalignant esophagobronchial fistulas are rarely observed. Ribbert has suggested a developmental origin, but it is generally agreed that they are usually secondary to traction diverticula caused by the healing of tuberculous lymph glands. Foreign bodies may occasionally be the cause. Death from pulmonary suppuration is almost certain to ensue unless the fistula is closed. It is surprising that the defect can be tolerated over a period of years, but a chronic course is not uncommon.

The condition is so rare that no one has had extensive experience in the treatment. In one case Clerf succeeded in closing the fistula by cauterizing its surfaces with silver nitrate through the esophagoscope. For several weeks subsequent to the procedure, feeding was done through a catheter passed into the stomach. In the case under consideration there are two factors which make it peculiar. These are the cardiospasm and what seems to be a large pulmonary cavity. The obstruction at the lower end of the esophagus and the dilatation of the esophagus must be important in favoring the patency of the fistula and the passage of food through it. Probably the first step in treatment should be to relieve the cardiac obstruction. The second should be an attempt to close the fistula by cauterization with silver nitrate. If these procedures are successful the pulmonary suppuration has still to be dealt with. Once the fistula is closed, this may improve sufficiently not to require treatment. Drainage of an abscess or lobectomy for bronchiectasis may be necessary.

The reproduction of the roentgenogram leaves uncertainty as to whether what seems to be a cavity in the lung is truly such a cavity or is barium in the fundus of the stomach which has been displaced upward by an elevated diaphragm.

If the cauterization fails to close the fistula, surgical closure must be attempted. The almost certain presence of extensive pleural adhesions makes the question whether the procedure could be performed extrapleurally or intrapleurally unimportant. Two surgical approaches can be conceived of: direct extrapleural exposure of the diverticulum without mobilization of the lung and mobilization of the lower lobe with coincidental exposure of the tract and lobectomy. In the first procedure two ribs directly posterior to the lesion should be resected through a paravertebral incision and the posterior mediastinum reached by dissecting the parietal pleura from the ribs and vertebral bodies. In the second procedure a long posterior segment of the eighth rib should be resected, the pleural cavity opened widely, the lung freed well to the hilus, the diverticulum located and closed, and a lobectomy performed. In either operation one would anticipate considerable difficulty in locating the diverticulum. A catheter inserted into the fistula through the esophagoscope shortly before the operation should help in localization.

### COLLES' FRACTURE AND TYPHOID

*To the Editor:*—A boy 14 years old was admitted to the hospital with Colles' fracture, which was sustained two weeks before. No treatment was administered for the fracture. The day after coming to the hospital he had a temperature of 101.4 F. Several days later a diagnosis of typhoid was made. What is your opinion as to the proper procedure? Should the fracture be reduced immediately or would it be advisable to wait until the typhoid subsides? What are the complications that may develop in such a case if the fracture is reduced?

MORTON J. EARLEY, M.D., Spangler, Pa.

**ANSWER.**—Healing of a Colles fracture in a 14 year old boy is so rapid that at the end of two weeks it is unlikely that much could be done in the way of a reduction without an open operation. If the deformity is not bad, readjustment will take place in a child of this age, giving a surprisingly good result without reduction. While typhoid patients stand a general anesthetic reasonably well, the general condition of the patient must be taken into consideration before undertaking even a closed reduction. Typhoid is a general blood infection and is occasionally followed by osteomyelitis. An open operation would be likely to be followed by infection and therefore should not be considered at the present time. The probabilities are that it would be much safer to leave the fracture entirely alone.

## NO DRUG TO INCREASE LYMPHOCYTES

*To the Editor.*—What drugs, if any, stimulate the lymphatic system so as to increase the number of lymphocytes in the blood stream? I have been unable to find any literature on the subject. Is there any drug that will stimulate the lymphocytes, as pentnucleotide does the polymorphonuclear cells?

I. L. CUTLER, M.D., Rutland, Mass.

**ANSWER.**—As far as is known there are no drugs that specifically stimulate the lymphatic system or the production of lymphocytes. Certain diseases, such as pertussis and infectious mononucleosis, are accompanied by a lymphocytosis, but the cause for this is not known.

## RELAPSING FEVER OR TULAREMIA

*To the Editor.*—A man aged 80 was visiting in the Teton Mountains in Wyoming in the early part of July. A few hours after carrying an armful of wood into the house he noticed on each arm what he thought were ticks. He went to the doctor in the community, who diagnosed his condition as "tick fever." The symptoms were fever, nausea, vomiting, numbness in both arms, elbows and wrists, numbness of the right leg and pain in the back of the neck and in the back. The temperature rose to 103 F. He came home and since that time soreness in the muscles and loss of appetite have persisted. There is elevation of temperature daily to 101 F. My diagnosis is relapsing fever. Could you supply me with the latest treatment of this condition?

M.D., Illinois.

**ANSWER.**—The symptoms presented by this patient are insufficient for a diagnosis of relapsing fever. In this disease there is an incubation period of from six to nine days between the infected tick bite and the onset of symptoms. The febrile stage lasts three days, followed by an afebrile period of four or five days.

Not all tick bites cause relapsing fever. Numerous persons in the region of Gold Park, Nev., have been bitten by ticks with no untoward consequences. Because of the daily elevation of temperature, tularemia should also be considered.

Diagnosis of relapsing fever rests on finding the spirochetes in a blood smear taken during the febrile stage. Smears should be stained with 20 per cent Giemsa stain for thirty minutes.

For treatment, neosphenamine is specific when given in sufficient doses during the period of rising temperature. The same dose as in antisyphilitic therapy is indicated. If inadequate amounts of the drug are used, relapses are more prone to recur.

## HUNTINGTON'S CHOREA

*To the Editor.*—What is the latest treatment for Huntington's chorea? Please list the literature supplementing this information.

MORTON M. STERN, Medical Student, Newark, N. J.

**ANSWER.**—A search of the literature published in the last five years does not reveal any articles dealing with the treatment of Huntington's chorea nor are there any suggestions as to treatment to be found in the discussion of this condition in the articles found in the late systems of medicine. This question was further taken up with several prominent neurologists and no knowledge of any new treatment was reported.

## PULMONARY TUBERCULOSIS IN LABORATORY WORKER

*To the Editor.*—A man aged 30 is now under treatment for pulmonary tuberculosis. Laboratory reports are positive; physical and x-ray examinations indicate a moderately advanced process with two small cavities in the apex of the right lung. The remainder of the lung appears clear. An exhaustive search of the family history and any possible outside contacts reveals nothing which would indicate a possible source of infection. The patient has worked for the last six years in a diagnostic laboratory doing a moderate number of positive sputum examinations. X-ray examinations of the chest four years ago revealed no evidence of pulmonary tuberculosis. Does pulmonary tuberculosis occur in laboratory technicians as a direct result of their work in a diagnostic laboratory making a moderate number of positive sputum examinations? If so, what is the percentage? What is the likelihood of a man aged 30, in apparent good physical health and having a negative chest roentgenogram, developing pulmonary tuberculosis as the result of his six years' work in a diagnostic laboratory? Could this case be termed an occupational disease under the workmen's compensation act?

EDWARD D. DAKE, M.D., Rome, N. Y.

**ANSWER.**—Since the patient is 30 years old and the x-ray examination of the chest four years ago revealed no evidence of pulmonary tuberculosis, one should also know whether he reacted to tuberculin at that time. A laboratory worker who makes examinations of sputum containing tubercle bacilli may easily contract an infection provided extreme care is not exercised. In the occasional case there is good evidence of the disease having been contracted in the laboratory; that is, non-reactors have become reactors while at work with no other known contact with tubercle bacilli and have later developed the disease clinically. Even then it is difficult to be certain that the infection was not contracted outside the laboratory. As

there are few places where large numbers of laboratory workers are employed, it is difficult to obtain sufficiently large figures to determine accurately what percentage fall ill from tuberculosis. In this case, if no tuberculin test was administered four years ago it would be impossible now to determine when the infection first developed; it may have been many years before the patient was employed in the diagnostic laboratory and the present manifestations could easily be the result of endogenous reinfection.

X-ray examinations of tuberculin reactors are of but little help in detecting the primary tuberculosis complex, since rarely does the roentgenogram reveal such complexes in more than 10 or 15 per cent of the reactors examined. Therefore, unless more evidence is available than negative x-ray observations four years ago, it would be a difficult matter to prove that this man's tuberculosis was contracted in the laboratory so as to be termed an occupational disease under the workmen's compensation act, unless the act in the state in which he resides specifically provides for the development of clinical disease while at work and does not take into consideration the possible earlier origin.

## GASTROINTESTINAL UPSETS AND CHLORINE IN DRINKING WATER

*To the Editor.*—Is it true that for many persons the drinking of chlorinated water leads to stomach and intestinal complaints? Is it true that in many localities people do not fully appreciate that this is the cause of repeated attacks of mild cramps, colic, belching and a host of indefinite gastrointestinal symptoms?

M.D., Minnesota.

**ANSWER.**—The accepted concentration of chlorine in the purification of water is one part in a million. Chlorine gas reacts with organic material and with water to form unstable hypochlorous acid. It is difficult to understand how such a low concentration of chlorine or chlorine compounds could cause digestive disturbances.

Whipple (*Microscopy of Drinking Water*, ed. 4, New York, John Wiley & Sons, 1927) states that:

The chlorination of waters which contain certain organic compounds in solution will cause tastes and odors of different characteristics and degrees of intensity depending upon the nature of the organic matter and its concentration. By-products, tastes and odors should be subdivided into:

A. Those caused by combination of chlorine and algae oils or other vegetable or animal matters.

B. Those resulting from chlorine and specific chemicals such as phenols and cresols.

An overdose of chlorine will mask the chlorophenol taste, but upon heating or otherwise driving off the "free" chlorine, the by-product taste still remains. The product is apparently of low volatility and stable, since boiling away 50 per cent of the sample fails to rid the water of the disagreeable taste.

It is perhaps possible that gastrointestinal upsets, such as flatulence, "sour stomach," constipation or diarrhea, might be due to chemical alterations, but it is much more likely that the chlorination has nothing to do with the disturbances. Many of these are of bacterial origin but are transmitted by way of infected food or by food handlers rather than by water. Another possibility is that inadequate chlorination may permit infections to be transmitted by way of the drinking water. The taste of chlorine leads to the false incrimination of the chlorine as the cause of the disturbance. Boiling the water drives off the "free" chlorine and also kills the bacteria.

## IRON INTRAVENOUSLY FOR ANEMIA

*To the Editor.*—I have been interested in the use of iron preparations administered intravenously in the treatment of hypochromic anemias. Could you give me some information as to their use and their reactions and whether they have or have not been considered by the Council on Pharmacy and Chemistry?

MURRAY W. SHULMAN, M.D., Newark, N. J.

**ANSWER.**—The intravenous or intramuscular administration of iron in hypochromic anemia is to be condemned in all but extraordinary circumstances. If given in adequate amounts to cure the anemia, it is painful, toxic, dangerous and expensive. Heath and Patek (*Medicine* 16:267 [Sept.] 1937) state that they have never seen a case that responded to parenteral iron which failed to respond equally well to adequate dosage by mouth. (Failure to obtain results with iron by mouth is usually due to inadequate dosage.) Only in cases in which severe diarrhea or some other serious contraindication to oral therapy exists should parenteral treatment be considered. While the Council has accepted one iron preparation for injection (green iron and ammonium citrate, U. S. P.), it is stated in connection with the Actions and Uses as given in New and Nonofficial Remedies that "the Council is not convinced that the intra-

muscular or hypodermic administration of iron yields effects which differ from those obtained by the oral administration; however, the unsettled state of iron therapy and the rather large clinical use of iron by intramuscular or subcutaneous injection appears to justify the provisional acceptance of this preparation."

#### CHILLS AND FEVER AFTER STRENUOUS PHYSICAL TRAINING

To the Editor:—A man aged 24, weighing 150 pounds (68 Kg.) and 5 feet 10 inches (178 cm.) in height, had been training extensively for two months prior to a track meet, running between 2 and 3 miles plus calisthenics daily, working at the same time from 5 p. m. to 1 a. m. The days before the meet he had fever, chills and a clammy cold sweat over his body lasting for several minutes. July 3, the next day, physical examination was negative, but the development of an afternoon temperature from 101 to 103 F. daily kept him in bed. The hemoglobin was 90 per cent, red cells 5,400,000, white cells 8,000, polymorphonuclear leukocytes 74 per cent, lymphocytes 24 per cent, monocytes 2 per cent. Tests for malaria, syphilis, undulant fever and typhoid were negative. The urine was normal. No focus of infection was found. Pleurisy developed about two weeks after the onset of the first symptoms and a pleural tap was negative and recovery complete. At odd intervals chills and fever would return in one attack and he would be apparently well between them. Could this have been a syndrome precipitated by intensive training or is it possible for a focus of infection to remain "hidden" for so long a period with no other outward signs?

W. A. BALOGH, M.D., Dunellen, N. J.

ANSWER.—The data are, of course, insufficient to permit one to arrive at a diagnosis, but in answering the specific questions raised one would suggest that the illness was probably precipitated by the intensive training and incident exhaustion with a presumed "lowered resistance." On the other hand, certain experiments in animals have shown that extreme fatigue paradoxically seems to increase the resistance to deliberate infection. It is indeed possible for a focus of infection (not necessarily in the sites usually associated with the term) to exist. The history of fever and pleurisy suggests that such a focus may be tuberculous and studies with the roentgenograms, skin test with purified protein derivative, sedimentation rate of the red cells and repeated careful examinations should be made. The weight should be registered regularly. Other evidence of infection must also be sought, particularly in the urethra and prostate.

#### POSSIBLE ALLERGY TO CATGUT

To the Editor:—Several years ago a patient was operated on for streptococcal salpingitis, cystic ovaries and chronic appendicitis. A suspension of the uterus was also done. The sutures used were chromicized sheepgut, no silk or linen sutures being used, and clips were used to close the skin. Before this time she had no allergy of any sort, but since then, beginning about four months after the operation, she has had chronic hives, especially on the lower half of the body. She attributed these at first to potatoes and found some relief by abstinence from them. Lately the condition has become more severe, especially if clothing made of wool or partly of wool is worn and if lamb or mutton is eaten. Could she have developed an allergic reaction to the sutures left in the body? How could an extract or testing solution be made for a skin test? Since the operation she has become more obese; she weighed 185 pounds (84 Kg.) before and 200 pounds (91 Kg.) after it. Diet and small doses of thyroid brought this weight down to 175 pounds (79 Kg.) in several months.

M.D., Pennsylvania.

ANSWER.—The question of sensitivity to catgut is still in dispute. A number of clinical studies of probable catgut allergy have been reported (Hinton, J. W.: *Arch. Surg.* 33:197 [Aug.] 1936. Tripp, H. D.: *J. Indiana M. A.* 28:383 [Aug.] 1935. Kraissl, C. J.: *Surg., Gynec. & Obst.* 63:561 [Nov.] 1936). Animal experiments, however, have generally failed to confirm the claim that catgut is antigenic (Marconi, L.: *Rassegna internaz. di clin. e terap.* 14:3, 1933. Friagioni, P.: *Arch. ital. de chir.* 43:334, 1936). The antigenic relationship between catgut and sheep serum could not be demonstrated by Marchesani in animal experiments (*Ber. re. d. Versamml. d. Deutsche Epth. Gesellsch.* 49:233, 1932).

In the case mentioned the following considerations are against the urticaria being due to catgut: 1. Sensitization to chromicized catgut because of its relative resistance to digestion is even less likely than to ordinary catgut. 2. The intermission of four months before the development of urticaria is unlikely as an incubation period because of the length of time. 3. The relationship of wool, lamb or mutton to catgut (sheep intestine which has, however, been greatly altered in its preparation as chromicized catgut) is not established. Wool sensitive patients are not usually sensitive to lamb, and vice versa.

The other more common causes of urticaria (drug sensitization, food sensitization, endocrine disturbance, foci of infection) should be considered first in this patient. However, if it is

desired to prepare an extract of chromicized gut, it should be ground thoroughly in a mortar with sand, extracted with physiologic solution of sodium chloride for several days and sterilized by filtration through a bacterium retaining filter. The material may then be tried without dilution and in various dilutions (1:10, 1:100, 1:1,000) by the intradermal method in the patient. A number of "normals" should be tested likewise to ascertain that the extract in the concentration used is not irritating to the normal skin (false positive reaction).

#### REINJECTION OF ASCITIC FLUID IN CIRRHOSIS

To the Editor:—Is it an approved procedure to reinject intravenously in moderate sized doses (about 500 cc.) ascitic fluid removed in a case of portal cirrhosis? The fluid would be collected aseptically. Isn't the loss of the protein in the fluid, which in this case amounts to from 5 to 18 liters (quarts) every two weeks, a drain on the patient which might be lessened by reinjection?

M.D., Virginia.

ANSWER.—This procedure has been carried out in the past by several investigators in cases of cirrhotic ascites with conflicting results. Most ascitic fluid of this nature contains less than 1 per cent of protein and the colloid osmotic pressure is usually low. It is true that such a daily loss of protein is a serious drain on the patient's reserves; but many cases have been followed over long periods with frequent determination of the serum protein values at stated intervals and in spite of the large loss of protein in the ascitic accumulations these patients are able to keep the serum protein at a fairly constant though subnormal level. In order to get enough protein from ascitic fluid it would necessitate parenteral administration in extremely large amounts. Cumulative experience in this field seems to have demonstrated the fact that repeated blood transfusion and the administration of 6 per cent acacia will more favorably affect the protein content and colloid osmotic pressure than would the injection of protein by the method suggested.

#### NITROUS OXIDE ANALGESIA

To the Editor:—Do you recommend an anesthetic machine of the Ohio Analgesor type for minor operations such as opening an abscess? Ethyl chloride is all right for the skin but does not relieve the pain of probing. Would some type of glass container of chloroform as used in obstetrics for self administration give adequate relief from pain with safety?

ALEXANDER WINTER, M.D., New York.

ANSWER.—Many minor surgical procedures, such as opening abscesses, may be efficiently carried out under nitrous oxide analgesia. The Ohio Analgesor is a type of apparatus designed for producing nitrous oxide analgesia (not anesthesia) by means of self administration. This apparatus mixes nitrous oxide with air and should be operated by the patient. Attempts to produce anesthesia with this instrument will result in oxygen want. By self administration, satisfactory analgesia is produced in many cases.

Self administration of chloroform has been deemed unwise by many because of the toxicity of the drug even in small quantities. If the quantity of the drug administered is controlled carefully and adequately, it may be used with relative safety. Self administration, as suggested, does not offer adequate control of the quantity inhaled in the majority of cases.

No anesthetic agent, apparatus or technic can be recommended. However, individuals may be recommended for the administration of anesthetic agents. The safety of any drug or method in medicine is largely dependent on the doctor's knowledge of it.

#### COITUS DURING ANTISYPHILITIC TREATMENT

To the Editor:—I am treating a man and his wife for syphilis. Both patients have had two and a fraction courses of nearsphenamine (about nineteen injections) and one course of bismuth preparations. They intend to continue treatment. Is it possible or likely that one patient would be cured before the other and that the uncured partner would reinfect the other? No measures for prevention of infection have been used during intercourse. Is it necessary that coitus be curtailed? M.D., Illinois.

ANSWER.—When both husband and wife are infected with syphilis, no curtailment of intercourse is necessary except so far as contraceptive measures may be desirable for the prevention of pregnancy. It is unwise for a woman with early syphilis to undertake pregnancy until at least a year of treatment has been given.

It is improbable that one patient will be cured before the other and subsequently reinfect the uncured partner. It has happened that both partners have been cured and that one has subsequently been reinfecting from an outside source and has then reinfecting the other partner.



## INFRA-RED PHOTOGRAPHY AND MALIGNANT CONDITIONS

*To the Editor:*—In a recent article in Collier's the use of infra-red photography was mentioned as a means of determining the extent of inward growth of tumors appearing in or just beneath the skin. The author stated also that such means give an indication of possible malignant conditions. What is the status of such work? If it is of any value, experimental or otherwise, please outline the technique or cite references.

M.D., North Carolina.

**ANSWER.**—It is possible by means of infra-red photography to visualize the superficial veins in the skin of subcutaneous tissues. This procedure does not permit a distinction between a benign and a malignant tumor. In its present stage of development it has no value in the diagnosis of neoplastic diseases.

SIMILAC, ORANGE JUICE AND COD LIVER OIL  
IN INFANT FEEDING

*To the Editor:*—Since birth a baby has been on a diluted similac formula exclusively. Is this a satisfactory substitute for a whole milk formula over an extended period of time? When should orange juice and cod liver oil be started? The child is now 3 weeks old and has gained nicely.

ALVIN ROSENBERG, M.D., Morristown, N. J.

**ANSWER.**—Similac in dilutions as recommended at different ages by the manufacturer makes a good formula. It is a satisfactory substitute for a whole milk formula until about 4 or 5 months of age. Orange juice and cod liver oil should be started now, as the infant is nearing 4 weeks of age.

## ICE CREAM FOR CHILDREN

*To the Editor:*—What is considered the proper time to introduce ice cream into the diet of a child? I can find no satisfactory statement on this point in any books to which I have access.

M.D., New York.

**ANSWER.**—Ice cream is a frozen, sweetened milk product, most often made with the addition of some flavoring extract. If this frozen material is properly prepared and protected against spoiling, it may be given in small quantities to children starting at 18 months or 2 years of age. A caution should be urged that the product be of the purest quality.

## TESTES ATROPHY AND TESTICULAR EXTRACTS

*To the Editor:*—When testicular extracts are administered in the treatment of the benign prostate hypertrophy or chronic prostatitis is there any danger of producing a secondary atrophy of any of the component cells of the testis in the patient under treatment?

M.D., Idaho.

**ANSWER.**—There is probably no danger. In immature rats such substances cause severe testicular injury but in mature rats no such effects have been reported. No reports of damage to testes have been reported for man.

ACTION OF MAGNESIUM SULFATE SOLUTIONS  
SUBCUTANEOUSLY

*To the Editor:*—Please explain why a 50 per cent solution of magnesium sulfate, although hypertonic, is painless when injected subcutaneously.

M.D., Indiana.

**ANSWER.**—A solution of magnesium sulfate in the concentration of 0.8 per cent is capable of producing local anesthesia when injected subcutaneously. At this concentration it acts slowly. When the concentration is 50 per cent the action is almost instantaneous, the anesthesia being produced by the action of the drug on the nerve endings and the nerve trunks. Consequently a subcutaneous injection of a 50 per cent solution of magnesium sulfate is painless.

## THE SKELETON AND BODY WEIGHT

*To the Editor:*—To what degree is weight affected by difference in the weight of the skeleton? For instance, what difference in weight would one expect in three men of the same age and same height, one having a frame that would be called heavy, another medium and another light?

W. S. DOUGLAS, M.D., Lewiston, Idaho.

**ANSWER.**—These queries cannot as yet be answered categorically; there are not enough relevant observations. What may be said definitely is as follows:

The skeletons of persons who have died of prolonged exhaustive illness are as a rule lighter than those of persons of the same age and development who have not been so affected.

In senility the skeleton gradually loses in weight, and in some instances the eventual loss may be considerable. But there is little if any regularity to the process.

During adult life, under normal conditions, the weight of the skeleton is proportionate to the height and robustness of the person. But even here, as in all other features of the human body, there is a range of normal individual variation.

PARALYSIS OF ARM AFTER TIGHT BANDS  
OR BRACES

*To the Editor:*—What are the possible effects of shoulder braces or arm bands in causing "peripheral nerve lesions of the arm and forearm"? What procedures are indicated to prevent such injuries?

GREGORY SMITH, M.D., New York.

**ANSWER.**—Shoulder braces that are too tight may induce sensory and motor paralyzes of the extremity of varying degrees. "Crutch paralysis" is of the same character and may last for some weeks. The treatment consists of removal of the cause, such as too tight shoulder braces or bands, and complete recovery may be predicted.

## VEHICLE FOR BROMIDES AND BELLADONNA

*To the Editor:*—Can antipyrine, bromides and tincture of belladonna be combined in a single prescription for whooping cough? I have used the latter two together in a vehicle of syrup of citric acid and cinnamon water, which, however, does not make a pleasant tasting preparation. Could the three be combined in syrup of glycyrrhiza? Is there something better?

M.D., Iowa.

**ANSWER.**—Antipyrine, bromides and tincture of belladonna may be combined in a single prescription, and the syrup of glycyrrhiza makes a better vehicle for them, as far as disguising the taste is concerned, than does syrup of citric acid and cinnamon water. There is probably no better vehicle for these drugs than syrup of glycyrrhiza.

## FAMILIAL SPINAL SPASTIC PARAPLEGIA

*To the Editor:*—I should like information or references as to any arrestive or preventive medical treatment for familial spinal spastic paraplegia.

M.D., Pennsylvania.

**ANSWER.**—There is no known treatment that will arrest the course of this disorder. Like other familial diseases, it might ultimately be stamped out if those afflicted should be sterilized.

## HAVERHILL FEVER

*To the Editor:*—Who is equipped to do an agglutination test for Haverhill fever? Kindly give bibliography of this disease.

E. C. ALEXANDER, M.D., Castalia, Ohio.

**ANSWER.**—Agglutination tests for Haverhill fever can be done at the Division of Infectious Diseases, National Institute of Health, Washington, D. C. Dr. Place at the Boston City Hospital is also equipped to do this test. The following references give a good description of the disease:

- Scharles, F. H., and Seastone, C. V.: Haverhill Fever Following Rat Bite, *New England J. Med.* 211:711 (Oct. 18) 1934.  
Parker, Frederic, Jr., and Hudson, N. P.: The Etiology of Haverhill Fever (Erythema Arthriticum Epidemicum), *Am. J. Path.* 2:357 (Sept.) 1926.  
Place, E. H.; Sutton, L. E., Jr., and Willner, Otto: Erythema Arthriticum Epidemicum, Preliminary Report, *Boston M. & S. J.* 194:285 (Feb. 18) 1926.  
Hazard, J. B., and Goodkind, Robert: Haverhill Fever (Erythema Arthriticum Epidemicum), *THE JOURNAL*, Aug. 13, 1932, p. 534.

## GARLIC TO LOWER BLOOD PRESSURE

*To the Editor:*—Is the use of "garlic" of any value in lowering blood pressure in essential hypertension?

M.D., South Carolina.

**ANSWER.**—No.

## TREATMENT OF HEMANGIOMA

*To the Editor:*—With regard to "Treatment of Hemangioma," page 1683 of *THE JOURNAL*, Oct. 29, 1933, I should like to suggest a source of solid carbon dioxide available to any practitioner. Not having a cylinder to make carbon dioxide snow, I decided to use commercial dry ice and obtained some from my druggist. Cutting it into appropriate shapes and sizes, I have used it to cure successfully three hemangiomas. The first patient was a baby girl of six months with two pea sized hemangiomas, one in the center of the forehead and the other on the inner aspect of the thigh. The other patient was a girl of six with a smaller spider-like hemangioma on her temple. All were cured without scarring with one fifteen second application each.

FREDERIC SPEER, M.D., Kansas City, Kan.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, Jan. 3-5 and June 20-22. Sec., Dr. J. N. Baker, 517 Dexter Ave., Montgomery.

ALASKA: Juneau, March 2. Sec., Dr. W. W. Council, Box 561, Juneau.

ARIZONA: *Basic Science*. Tucson, Dec. 20. Sec., Dr. Robert L. Nugent, Science Hall, University of Arizona, Tucson.

COLORADO: Denver, Jan. 4-6. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT: *Basic Science*. New Haven, Feb. 11. Prerequisite to license examination. Address State Board of Healing Arts, 1895 Yale Station, New Haven.

DELAWARE: Dover, July 11-13. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science*. Washington, Dec. 26-27. *Medical*. Washington, Jan. 9-10. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

GEORGIA: Atlanta, June. Joint-Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

HAWAII: Honolulu, Jan. 9-12. Sec., Dr. James A. Morgan, 48 Young Bldg., Honolulu.

IDAHO: Boise, April 4-7. Dir., Bureau of Occupational License, Mr. D. B. Cruikshank, Rm. 355, State Capitol Bldg., Boise.

ILLINOIS: Chicago, Jan. 24-26. Superintendent of Registration, Department of Registration and Education, Mr. Homer J. Byrd, Springfield.

INDIANA: Indianapolis, June 20-22. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

IOWA: *Basic Science*. Des Moines, Jan. 10. Dir., Division of License and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MICHIGAN: Ann Arbor and Detroit, June 14-16. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 100 W. Allegan St., Lansing.

MINNESOTA: *Basic Science*. Minneapolis, Jan. 3-4. Sec., Dr. J. Charney McKinley, 126 Millard Hall University of Minnesota, Minneapolis. *Medical*. Minneapolis, Jan. 17-19. Sec., Dr. Julian F. DuBois, 350 St. Peter St., St. Paul.

MONTANA: Helena, April 4-5. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEBRASKA: *Basic Science*. Omaha, Jan. 10-11. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEVADA: *Reciprocity and oral examination*. Carson City, Feb. 6. Sec., Dr. John E. Worden, Capitol Bldg., Carson City.

NEW HAMPSHIRE: Concord, March 9-10. Sec., Board of Registration in Medicine, Dr. Fred E. Clow, State House, Concord.

NEW JERSEY: Trenton, June 20-21. Address, Dr. William L. Wilbur, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, April. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 23-26. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, 315 Education Bldg., Albany.

NORTH CAROLINA: Raleigh, June 19. Sec., Dr. William D. James, The Hamlet Hospital, Hamlet.

NORTH DAKOTA: Grand Forks, Jan. 3-6. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

PENNSYLVANIA: Philadelphia, Jan. 3-7. Sec., Board of Medical Education and Licensure, Dr. James A. Newpher, 400 Education Bldg., Harrisburg.

PUERTO RICO: San Juan, March 7. Sec., Dr. O. Costa Mandry, Department of Health, San Juan.

RHODE ISLAND: Providence, Jan. 5-6. Chief, Division of Examiners, Mr. Robert D. Wholey, 366 State Office Bldg., Providence.

SOUTH DAKOTA: Pierre, Jan. 17-18. Director of Medical Licensure, Dr. B. A. Dyer, State Board of Health, Pierre.

VERMONT: Burlington, Feb. 14. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

WASHINGTON: *Basic Science*. Seattle, Jan. 5-6. *Medical*. Seattle, Jan. 9-11. Dir., Department of Licenses, Mr. Harry C. Huse, Olympia.

WISCONSIN: Madison, Jan. 10-14. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

WYOMING: Cheyenne, Feb. 6. Sec., Dr. G. M. Anderson, Capit. Bldg., Cheyenne.

NATIONAL BOARD OF MEDICAL EXAMINERS  
SPECIAL BOARDS

Examinations of the National Board of Medical Examiners and Special Boards were published in THE JOURNAL, December 3, page 2141.

California June Examination

Dr. Charles B. Pinkham, secretary, California State Board of Medical Examiners, reports the written examination held at San Francisco, June 28-30, 1938. The examination covered nine subjects and included ninety questions. An average of 75 per cent was required to pass. One hundred and seventy-four candidates were examined, 172 of whom passed and two failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists.....(1937)	78.9, 80.3, 80.7, 82.4, 83.7, 83.8, 84.2, 84.3, 85.1, 87, 87.7		77.7.
Stanford University School of Medicine.....(1938)	78.1, 78.2, 78.6, 79, 79.1, 79.4, 80.6, 80.7, 80.8, 81, 81.1, 81.2, 81.3, 81.3, 82, 82.1, 82.6, 82.6, 82.7, 82.8, 83, 83.3, 83.4, 83.4, 83.6, 83.8, 83.8, 84, 84.3, 84.3, 84.3, 84.6, 84.7, 85.1, 85.1, 85.1, 85.2, 85.3, 85.7, 86.1, 86.2, 86.6, 86.7, 86.8, 87.2, 87.2, 87.3, 88.3, 88.3, 89.3, 89.7, 92.1		76.6.

University of California Medical School.....	(1938)	77.2,
77.6, 77.8, 78.4, 80, 80.3, 80.3, 80.4, 81.1, 81.2, 81.7,		
82.1, 82.1, 82.2, 82.3, 82.4, 82.6, 82.7, 82.8, 83.2, 83.4,		
83.7, 83.8, 84, 84.4, 84.6, 84.6, 84.7, 84.7, 84.8, 84.8,		
84.9, 85.2, 85.3, 85.4, 85.4, 85.7, 86.1, 86.2, 87, 87.4,		
87.6, 87.7, 87.8, 88, 88.8, 89.6, 89.7, 90.4		
University of Southern California School of Medicine.....	(1938)	79.2,
82.3, 82.9, 83.1, 83.2, 83.4, 84.1, 84.3, 86.4, 87.3, 88.7		
University of Colorado School of Medicine.....	(1937)	77.6, 85.3
Northwestern University Medical School.....	(1924)	83.3, (1938)
Rush Medical College.....	(1923)	89.4
(1937) 79.9, 80.9, 82.3, 86.7, (1938) 85.9, 86.4		86.1,
School of Medicine of the Division of Biological Sciences.....	(1937)	83.8
University of Illinois College of Medicine.....	(1938)	81.8
State University of Iowa College of Medicine.....	(1936)	81.2,
(1937) 80		
University of Louisville School of Medicine.....	(1936)	79.4
St. Louis University School of Medicine.....	(1937)	76.9,
78.7, 85.8, (1938) 82.4, 86.2		
Creighton University School of Medicine.....	(1937)	79.7,
80.1, 80.8, 81.3, 83.8, (1938) 79.1, 85.4		
University of Nebraska College of Medicine.....	(1937)	80.6
Columbia University College of Physicians and Surgeons.....	(1937)	81.7
Long Island College of Medicine.....	(1937)	81.8
New York Medical College and Flower Hospital.....	(1937)	87.7
Duke University School of Medicine.....	(1936)	80.8
University of Oklahoma School of Medicine.....	(1937)	78.4
University of Oregon Medical School.....	(1936) 86.8, (1937)	87.7
University of Pennsylvania School of Medicine.....	(1936) 85.1, 86.8	
Marquette University School of Medicine.....	(1938) 81.3, 83.6	
University of Wisconsin Medical School.....	(1937)	85.7
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin.....	(1920) 80.8, (1926)	83.4
Ludwig-Maximilians-Universität Medizinische Fakultät, München.....	(1912)	78
Universität Heidelberg Medizinische Fakultät.....	(1912)	96.7
School	FAILED	Year Per Cent
University of California Medical School.....	(1938)	74.7
Schlesische - Friedrich-Wilhelms-Universität Medizinische Fakultät, Breslau.....	(1925)	65.7

Book Notices

Health Insurance with Medical Care: The British Experience. By Douglass W. Orr, M.D., and Jean Walker Orr. Cloth. Price, \$2.50. Pp. 271. New York: Macmillan Company, 1938.

An entertaining style and numerous personal illustrations and observations make this book easy reading and illuminative of many sides of the problem of medical care in England. There is also a full treatment of the health activities in England largely based on the "Report on the British Health Services" by PEP (Political and Economic Planning) which presents a much more rounded picture than has been given in previous discussions.

The one contribution which the reader has a right to expect from the first extensive work on this subject by an American physician is an evaluation of the medical service given under health insurance. There is an elaborate attempt to give such an evaluation but it can scarcely be said to be successful.

The key to the entire attitude of the book is found in the statement concerning the sources of information. The authors state that they "arrived well armed with introductions to Big Names in English medicine" but that when they talked with an official of the British Medical Association and showed him their list of names he told them to "use them, but they aren't typical" and added "Let me give you names of men who are in general practice and who have insurance panels; they know the system inside and out." The authors congratulate themselves that "Thus Dr. Hill steered us around a common pit-fall." The naiveté of this observation is revealing to any one who has undertaken research in Europe concerning social institutions—he is always met by persons who are anxious to show him around and to guide him to the "proper" sources of information; these are often persons who will present the facts that will most surely support the system. That is clearly what happened to the authors of this book.

One of their first informants said he had never "heard of any one getting favors from the doctors or otherwise taking advantage of the scheme." It must have required careful isolation to keep from finding persons who have heard of such things, because they are complained of in official documents and in medical journals and are topics of conversation almost everywhere. In spite of being so carefully guarded, the investigators seem to have run into some of this information, for they say "Some doctors may be hoodwinked or cajoled into

certifying patients as incapable of work when in reality they should not be certified; some may find it profitable to be known as an 'easy doctor.' Of "sick visitors" we are told that "protection of funds against malingerers is the sole motive" of their visits. The familiar statement that few visits are made by regional medical officers "to inquire into excessive prescribing" and "in only six cases were fines imposed" fails to tell of the continuous flood of letters that are sent out by these regional medical officers politely and mildly warning physicians against such prescribing, and of course nothing is said of the many complaints in official reports, including those of the Ministry of Health, of the excessive prescribing as the result of the efforts of the physician to satisfy the demands of the patient for what British physicians in their own journals frequently admit are unnecessary medicines.

We are informed that "those who assert . . . that N. H. I. has increased the burden of sickness or dodged its responsibility by shifting it to the voluntary hospitals are misrepresenting the facts" (page 85). Yet we are told only two pages earlier that one investigator "found several two to three hundred bed hospitals with waiting lists of five to six hundred each." It must have been difficult even to ride along the roads of England and not see the repeated appeals for financial aid for hospitals and not to be told continuously that this was largely due to the increased burden created by national health insurance.

Perhaps the sharpest criticism which can be directed against the authors is that they base their main arguments as to the good quality of the medical service on the statements of patients. Certainly no physician in this country would accept the fact that a quack or distributor of nostrums can produce thousands of testimonials to the efficiency of his services or of the panacea sold as proof that these were of value to the patient. Yet that is essentially the sort of evidence which is offered here. Certainly, any physician undertaking an experiment with any method of treatment would be expected to produce vital statistics as one measure of the success of his plan. This measure is almost entirely omitted. The statement that "in Britain national concern over a maternal mortality rate which nevertheless averages considerably lower than that of the United States has provoked vigorous action" is not justified in view of the fact that the maternal mortality rate for England was 41.1 per thousand, for Wales 55.7 and for Scotland 63.7, as an average for the years 1924-1933 (Report on Maternal Mortality in Wales, Ministry of Health, London, 1937) while, in the United States, Rhode Island, Wisconsin, Minnesota and several other states show a rate approximately the same as that of England and nearly all the states at all comparable as to climate and racial conditions show rates lower than Wales or Scotland (Vital Statistics—Special Reports 5:43 [March 1] 1938, Department of Commerce, Bureau of the Census, Washington, D. C.). The impression is conveyed that a 40 per cent decline in the death rate during the last forty years in London is in some way related to sickness insurance. The decline in the United States has been even greater, without sickness insurance.

The authors quote "one of the most authoritative persons we interviewed" as concluding that "a panel of 2,500 is not too many for a doctor who has also some private practice." The statistics presented by the British Medical Association in a recent discussion of the capitation rates of payment for physicians showed that a little over five combined office and house calls per insured person were required annually. A panel of 2,500 would require 12,500 such services a year, or about forty for each working day. Considering that other studies of the British health insurance system have shown that these services are much more numerous in certain seasons than in others, we gain a rather peculiar idea of the standard of good service which the authors must have had in view. If we were to use their own figures, which are as much in error as some of their conclusions, this calculation would show much worse conditions, because they quote one of their medical authorities who thinks that panel patients average about ten visits a year. It is strange that authors who say so much about the thoroughness of their investigation and publish so long a list of

persons interviewed and so extensive a bibliography did not check these statements with available official statistics.

The bibliography itself requires some little attention. The list of "pamphlets and reports" consulted omits the "Report by the Government Actuary on an Examination of the Sickness and Disablement Experience of a Group of Approved Societies in the period 1921-27" and also the "Report on Incapacitating Sickness in the Insured Population of Scotland during the year 1st July 1934 to 30th June 1935." Is it possible that this omission is due to the fact that these official reports contradict many of the conclusions of the book as to the character of the service given? The entire bibliography is principally noteworthy for its complete omission of a considerable number of books that have been published in Great Britain criticizing health insurance.

There is frequent reference to the way in which disease is supposed to be prevented by early attendance under sickness insurance. No mention is made of Scottish and British reports which complain that immunization for diphtheria lags behind American standards. The authors could have found much information contradicting their statements as to this feature of British health insurance by an examination of the "First Lecture of a London Postgraduate Course" on "Preventive Treatment and the General Practitioner" contained in the Supplement to the *British Medical Journal* for April 1938 as well as in numerous other publications favorable to health insurance. The difficulty which it is claimed existed in finding any opponents or antagonistic critics might have been overcome by a consultation of the correspondence columns of the *British Medical Journal* and the *London Lancet*.

Finally, the attempt to show that British health insurance conforms to the "ten principles" of the American Medical Association is a heavy strain on both facts and logic.

*The Doctrine of Signatures: A Defence of Theory in Medicine.* By Scott Buchanan. Cloth. Price, \$2.75. Pp. 205. New York: Harcourt, Brace & Company; London: Kegan Paul, Trench, Trubner & Co., Ltd. 1938.

This volume in the International Library of Psychology, Philosophy and Scientific Method under the editorship of Prof. C. K. Ogden of Cambridge University belongs in section C devoted to scientific method. In it a metaphysician prescribes a program for physic. He reverts to the classics, in which philosophy had a leading part, and shows how Plato, Aristotle and Galen established the demonstrative power of form and matter in the biologic and medical sciences, and pleads that its rediscovery and reestablishment in modern signatures would reinvigorate medical thinking and open new paths for released speculative energies now thwarted by the lack of an organized philosophy of medicine.

The doctrine of signatures assumes that the data of science are potential symbols and it calls on the liberal arts and sciences to develop, clarify and realize the potentialities of human observations. The practice of these arts and sciences ends in the discovery and formulation of abstract form through which the data achieve their status as facts and scientific evidence. Forms are not only what the signatures signify, they are also the causes of things and therefore the proximate subject matter of science. The author proceeds to show how Plato, Aristotle and Galen elaborated this theme and he ultimately arrives at teleology in Galen. This he interprets as none other than the principle of causal determinism of modern science explained and stated in its fulness in the light of its metaphysical implications. He urges physicians to familiarize themselves with Galen's philosophy of medicine and his concept of physiology, which may be summed up in the title of one of his chapters, *The Human Body as Artist*.

He has a vision of a fusion of interests of medical men and philosophers in cooperation in establishing a new and more rational organization of scientific thought that has a basis broad enough to include in its scope not only the therapeutic approach to disease but the ramifications of this rationally organized science into legal, social and religious fields. The central position of the medical sciences with reference to man offers inviting prospects of leadership to the organizers of

such a system of thought. "Physic should recover its lost humanism and its intelligibility *quoad nos* as well as *secundum se*."

The proposed program includes the following suggestions, the accomplishment of which in a number of instances is at least in the early stages of formulation or even accomplishment: A critical evaluation of the sciences on which the medical arts depend with special attention to their past uses and their possible future relevance to an integrated science of physic. The abstraction and reformulation of the first principles in these sciences, showing their subordination or interdependence inside a single science. A digest of current working hypotheses, instruments and technics in medical research and practice. A study of measurement in science, numerical and non-numerical. The construction of a rational science and an empirical science of physic based on the preceding studies. A study of medical casuistry, the applied sciences of medicine, diagnosis, prognosis, therapy. A study of social medicine, epidemics, preventive medicine, creative medicine, and the proposed agencies for the medical control of society and the social control of medicine. A study of the possibilities of a permanent board for the continuous criticism and codification of medical knowledge. The last proposal has in it the element of undesirable bureaucracy. Growing sciences do not lend themselves to lasting codification. A certain amount of helpful criticism can be secured through annual topical summaries by experts. An excellent feature in the sciences is found in annual summer conferences in which specialists meet for discussion of live topics, and conflicting views are exposed to criticism. A splendid example is the recently established Mikkelsen Foundation of Bergen, Norway, endowed by the statesman-diplomat who composed the political differences between Norway and Sweden. Its policy is to foster annual international gatherings of specialists in the various fields of the sciences and other forms of human intellectual activity for several weeks of common residence, round table discussions and mutual criticism, but without any commitments or decisions by the assembled body. In the field of medicine the annual gatherings appear to be dominated by professional and social trends rather than by those of the programs outlined. Useful as such gatherings are, there still may be a place for the quiet contemplation and discussion of the basic scientific and metaphysical aspects of physic which the author of these prolegomena of medicine has thought out.

**Voice for Speech.** By Frederick Wesley Orr, Professor of English and Director of the Division of Speech at the University of Washington. Cloth. Price, \$2. Pp. 283, with 17 illustrations. New York & London: McGraw-Hill Book Company, Inc., 1938.

The author states that his aim is to contribute in a broad sense to the education of the student and at the same time to attack specifically his voice problems in a basic, fundamental way. At the beginning he points out that "if the author has learned anything during the past ten years in regard to vocal training, it has been the necessity of discovering the cause of the vocal difficulty, whether it be in the thinking, the lack of emotional control, objectionable personality traits, or a defective vocal apparatus; and once the cause has been discovered, working specifically for the removal of that cause." His approach is both physiologic and psychologic, and he believes that any corrective program must take into consideration the entire personality of the individual: the physical condition of his vocal apparatus, its responsiveness to stimulation, and the interferences—including abnormal personality traits and bad vocal habits—which prevent a normal functioning. For purposes of study he divides the vocal apparatus into four different systems; the coordinating system, the breathing system, the tone initiating system and the tone modulating system. He devotes a section to each system, discussing its anatomy and physiology, the abnormalities in its functioning, and the methods of discovering such abnormalities as well as methods of establishing the normal. The remaining four sections are devoted to quality, pitch, duration and strength, and modulating tone into speech sounds. The author suggests a series of tests to determine the reliability of the physical apparatus, especially the sense organs, and in each section he gives a diagnostic chart so that

a record may be kept of the results of the tests made. A number of exercises and reading selections are also given in each section. The book covers a great deal of ground and is written with admirable simplicity. However, the arrangement of the material, with its many repetitive divisions and subdivisions, is somewhat complicated, although at the same time it has merit in that each section is a complete unit and, if so desired, can be studied entirely apart from the rest of the material. All in all, the book is a sensible one and to those interested in the subject it should prove useful.

**Spectrochemical Abstracts 1933-1937: Being a 52 Page Bibliography with Abstracts of Over 200 Papers on Spectrochemical Analysis.** By F. Twyman, F.Inst.P., F.R.S. Paper. Price, 4s. Pp. 52. London: Adam Hilger Limited, 1938.

Twyman is a personality in the field of spectroscopy and applied optical measurement. His spectrochemical abstracts compile the literature of spectroscopy during 1933-1937. There are fifteen pages of author references arranged alphabetically. The remaining thirty-four pages are classified into biologic material, earths, electrodes, gases, industrial materials, liquids, metals and alloys, minerals, nonmetals, oxides, precipitates, soils, apparatus, methods, general, and a list of books. Any active worker in spectroscopy has his own filing system. The value of Twyman's references lies in his careful selection of manuscripts. There are, of course, certain omissions of literature data and larger treatises on spectroscopy, but they will be noted by the modern spectroscopist. In general, the little brochure is a handy tool on the table of any scientific worker making use of spectroscopic apparatus.

**New Creations in Human Beings.** By Louis Berman, M.D. Cloth. Price, \$3. Pp. 316. New York: Doubleday, Doran & Company, Inc., 1938.

Those men who read Berman's book on glands and personality will be prepared to find in this volume the same mixture of science and what David Starr Jordan used to call *sciosophy*, or the shadow of wisdom. Again in this book Berman's thesis is that internal secretions have much to do with determining the character of the individual, so much so in fact that in many cases criminality can be cured by treating the patient with mixtures of desiccated glands.

Although no expert clinician would question the fact that persons suffering from glandular disturbances are inclined to be nervous, psychopathic and unhappy, few real experts in the field of glandular diseases would care to go so far as Berman does. One difficulty with Berman is that he has his own ideas of what constitutes the clinical picture of disturbances of function in glands such as the parathyroid and adrenal, ideas that do not coincide with those of most scientific physicians today. For instance, on page 41 he tells of a child brought to him because of her shyness, impulsiveness, "explosive assaultiveness," nervousness, poor appetite, insomnia, laziness and dulness at school. Because Berman found a low blood calcium he states categorically that all the girl's troubles were due to parathyroid insufficiency. He does not go on to say how beautifully she reformed on dried parathyroids swallowed three times a day.

On page 253 one finds a description of a burglar who was in and out of reformatories and Sing Sing for eighteen years. He had a persistent thymus gland; "the adrenals were rated as quite deficient, and the gonads and sex glands as moderately deficient." Another bad boy running around and getting into mischief had hyperthyroidism, persistent thymus and marked parathyroid deficiency. According to Berman "There is now a fair degree of certainty that the criminal has a combination of glandular disturbances as the background of his antisocial behavior" and that the way to get at the criminal diathesis is to eradicate these glandular disturbances in childhood.

After many sad experiences in practice, the reviewer cannot help wondering whether Berman's case of hyperthyroidism was diagnosed from a basal reading of +10 per cent, and the hyperparathyroidism from one blood calcium of 9 mg. reported by a careless, poorly trained technician. The reviewer happens to have seen several cases of serious parathyroid disease but he cannot remember having noted in the patients any great disturbance in character and certainly there was no sign of crimi-

nality. Actually, the patients were complaining of such things as a painful caving-in of the spine, polyuria or tetany. Similarly, the many patients seen by the reviewer with an adrenal tumor or Addison's disease did not show any criminal tendencies.

Berman's answer would probably be that the symptoms that he observes are those of early, mild and unrecognized changes in the glands, but the objection to that is that, if certain symptoms are not found when the disease is severe and recognizable, how can any one prove that they are characteristic of the disease in those early stages in which most experts would refuse to accept the diagnosis? We fear this book should be sold over the fiction counter.

## Bureau of Legal Medicine and Legislation

### MEDICOLEGAL ABSTRACTS

**Malpractice: Failure to Discover Disunion of Fracture.**—The plaintiff, a woman about 55 years old, injured her left hip Dec. 18, 1932. The next day, on the advice of her attending physician, the defendant, she was removed to a hospital, where roentgenograms disclosed an intracapsular fracture of the neck of the left femur. The defendant reduced the fracture and immobilized her left leg in a splint. Roentgenograms taken five days later showed that the fracture had been reduced satisfactorily. On Jan. 12, 1933, roentgenograms disclosed a bony union and that the fragments of bone were still in good alignment. The patient left the hospital Jan. 23, 1933. Two weeks later, about seven weeks after the injury, the defendant removed the splint and advised the plaintiff to get up and walk with the assistance of crutches. When she attempted to do so she exclaimed "My God, my hip isn't together, I can feel it grating," and then fainted. Although she repeatedly informed the defendant that she believed her "leg was not together," he failed to take or advise the taking of another roentgenogram. On June 15, 1933, the plaintiff went to a clinic, where roentgenograms showed disunion of the fragments of bone. An operation was subsequently performed by another physician, an orthopedic surgeon, but the end result was that she had a 50 to 75 per cent disability. She then sued the defendant for malpractice, the trial court directed a verdict in favor of the physician, and the court of appeals, Summit County, Ohio, affirmed the judgment rendered on the directed verdict. The case was then certified to the Supreme Court of Ohio.

In the judgment of the Supreme Court, the evidence showed that the bony union which takes place between fragments of bone following a proper reduction of a fracture of the neck of the femur may be followed by a disunion through absorption within a few weeks. Such disunion can be disclosed only by a roentgenogram. Accepted medical practice requires that a roentgenogram should be taken at the time the absorption can reasonably be expected to have taken place, if at all, to determine whether that absorption has occurred. In the instant case the defendant failed to take or advise the taking of roentgenograms when the plaintiff complained to him that she felt a grating sensation when she attempted to walk and that the fragments of bone were not together, which was at about the time an absorption might be expected to have taken place. The court was of the opinion, therefore, that the evidence was sufficient to warrant submission to the jury of the issue of the defendant's negligence.

But, continued the court, in order to recover damages the plaintiff must prove not only negligence or unskilfulness on the part of the defendant but also that his negligence or unskilfulness was the proximate cause of her injury. The uniting of fragments of a broken bone must be accomplished by the healing processes of nature and essentially there is always the possibility that nature will fail to achieve the desired result even when the attending physician has done properly everything known to surgical science. Similarly, if the physician's treatment has been unskilful or negligent and the broken parts fail to unite, there is also the possibility that the disunion would have resulted even had the physician used due care and skill. Proximate

cause in the present case was an ultimate fact to be proved by the plaintiff and, before the trial court could submit the case to the jury, there must have been evidence which would warrant the jury in drawing an inference of probability. There was, the court said, no such evidence in the record. In fact, the evidence showed that there was a lesser probability rather than a greater that bony reunion would have taken place.

The evidence showed, the court said, that the chance of reunion of the fragments of the bone on a remanipulation and resetting was lost because the defendant had let the patient go on walking with crutches for three months without taking a roentgenogram or giving other attention to the fracture. There was no evidence, however, to show that reunion would have taken place even with the best of treatment. The evidence was therefore insufficient, in the opinion of the court, to support an inference that if the chance had not been lost through the fault of the defendant the injury concerning which the plaintiff complained would not have occurred. Loss of chance of recovery, standing alone, is not an injury from which damages will flow.

Accordingly, the Supreme Court affirmed the judgment in favor of the defendant physician.—*Kuhn v. Banker (Ohio)*, 13 N. E. (2d) 242.

**Workmen's Compensation Acts: Compensability of Death from Strangulation of Preexisting Nonindustrial Hernia.**—From the strain and effort of lifting sacks of material in the performance of his duties, a loop of intestine was forced into the sac of an inguinal hernia from which the deceased already suffered. There the intestine became strangulated. In the course of an operation to release the strangulation, a general anesthetic was administered. Pneumonia followed and death ensued. The industrial accident board awarded compensation to the widow and minor daughter of the deceased. The plaintiff in this case, the employer's insurance carrier, sued to set aside that award. The trial court entered judgment in favor of the plaintiff insurance company, and when that judgment was reversed by the court of civil appeals of the second supreme judicial district, Texas, the insurance company appealed to the Supreme Court of Texas.

According to the pleading, said the court, the injury sustained by the deceased was in final analysis the strangulation of a part of his intestine. This strangulation resulted from the strain of lifting the sacks of material. The strangulation and the ensuing consequences fall clearly within the statutory definition of "injury." The preexisting hernia was incidentally involved in the occurrence of such an injury, but it did not itself constitute the injury or result from it. Nothing appears in the statute, said the court, on which to found a reasonable conclusion that the legislature intended to impose the limitations laid down by it on claims based on hernia, on any injury where no hernia is involved except a preexisting hernia which does nothing more than furnish a condition in which the force which causes the injury operates.

The judgment of the court of civil appeals, reversing the trial court's judgment and remanding the cause for trial, was therefore affirmed.—*Actna Life Ins. Co. v. Liles et al. (Texas)*, 114 S. W. (2d) 534.

## Society Proceedings

### COMING MEETINGS

- American Academy of Orthopedic Surgeons, Memphis, Tenn., Jan. 15-19.
- Dr. Carl E. Badgley, 1313 East Ann St., Ann Arbor, Mich., Secretary.
- American Association for the Study of Neoplastic Diseases, Baltimore, Dec. 28-30. Dr. Eugene R. Whitmore, 2139 Wyoming Avenue N.W., Washington, D. C., Secretary.
- American Student Health Association, New York, Dec. 29-30. Dr. Ruth E. Boynton, Students Health Service, University of Minnesota, Minneapolis, Secretary.
- Eastern Section, American Laryngological, Rhinological and Otolological Society, Boston, Jan. 11. Dr. Frank E. Kittredge, Masonic Temple, Nashua, N. H., Chairman.
- Middle Section, American Laryngological, Rhinological and Otolological Society, Sioux City, Iowa, Jan. 19-20. T. R. Gittins, Davidson Bldg., Sioux City, Iowa, Chairman.
- Southern Section, American Laryngological, Rhinological and Otolological Society, New Orleans, Jan. 14. Dr. Francis E. Lefebvre, Maison Blanche, New Orleans, Chairman.
- Western Section, American Laryngological, Rhinological and Otolological Society, Spokane, Wash., Jan. 29. Dr. Frederic G. Sprowl, Medical Arts Bldg., Spokane, Wash., Chairman.

## Current Medical Literature

### AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1928 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (\*) are abstracted below.

### American Journal of Medical Sciences, Philadelphia

196: 609-760 (Nov.) 1938

Protein Production and Exchange in Body Including Hemoglobin, Plasma Protein and Cell Protein. G. H. Whipple, Rochester, N. Y.—p. 609. Leukopenic Leukemia of Myeloblastic Type. F. R. Miller and W. B. Seymour, Cleveland.—p. 621.

Observations on Blood Regeneration in Man: III. Rise in Reticulocytes in Patients with Hematemesis or Melena from Peptic Ulcer. E. Schipdt, Copenhagen, Denmark.—p. 632.

Peritoneal Lavage in Treatment of Renal Insufficiency. J. E. Rhoads, Philadelphia.—p. 642.

Concentration of Individual Phosphatides (Lecithin, Kephalin, Ether-Insoluble Phosphatide) and of Cerebrosides in Plasma and Red Blood Cells in Pernicious Anemia Before and During Liver Treatment. E. Kirk, Copenhagen, Denmark.—p. 648.

Observations Made on Group of Employees with Duodenal Ulcer. Janette Jennison, New York.—p. 654.

Anorexia Nervosa and Pituitary Cachexia. W. J. Bruckner, C. H. Wies and P. H. Lavietes, New Haven, Conn.—p. 663.

Phenolphthalein Studies: Phenolphthalein in Jaundice. F. Steigmann, R. D. Barnard and J. M. Dyniewicz, Chicago.—p. 673.

\*Chronic Hypoglycemia: Problem in Carbohydrate Metabolism. S. Dorst, Cincinnati.—p. 688.

Pulmonary Pneumocyst: Report of Enormous Solitary Cyst in a Healthy Adult Female. G. Cheney and L. H. Garland, San Francisco.—p. 699.

Spontaneous Pneumothorax. J. J. Kirshner, Philadelphia.—p. 704.

\*Comparison of Etiology, Death Rates and Bacteremic Incidence in More Frequent Primary Pneumonias of Infants, Children and Adults. J. G. M. Bullova and M. Gleich, New York.—p. 709.

\*Benzedrine Sulfate in Persistent Hiccup: Report of Two Cases. M. S. Shaine, New York.—p. 715.

Standards for Maximal Reticulocyte Percentage After Intramuscular Liver Therapy in Pernicious Anemia. R. Isaacs and A. Friedman, Ann Arbor, Mich.—p. 718.

**Chronic Hypoglycemia.**—During a period of eighteen months Dorst observed sixty-two ambulatory patients who had low dextrose tolerance curves. From this it would seem that the existence of chronic hypoglycemia is far more common than is generally appreciated and that it frequently occurs in asthenic undernourished individuals who present the familiar picture of the "effort syndrome." The constantly low level of blood sugar may be responsible in part at least for the lack of vigor which characterizes these people, since the chief source of energy in mammalian metabolism is derived from the burning of carbohydrate. Patients with chronic hypoglycemia show a dextrose tolerance curve which remains in the fasting zone regardless of the ingestion of food and it is possible that under these conditions there is inadequate fuel to be suddenly expended in the form of energy. This syndrome must be differentiated from spontaneous hyperinsulinism. When treated with small doses of insulin (5 units before breakfast and 10 before lunch and dinner) a number of the patients with chronic hypoglycemia showed marked clinical improvement, an increase in the sense of well-being, gain in weight and increased appetite; concomitant with this improvement the dextrose tolerance curve returned to the usual normal configuration. The precise action of the insulin in effecting this change is not understood. The author suggests the possibility that the demobilization of hepatic glycogen is in some way inhibited and he hopes to establish this thesis by further investigation.

**Etiology, Death Rates and Bacteremia in Pneumonia.**—In this article Bullova and Gleich use the following terms to mean: infants as "children less than 2 years of age," children as "those from 2 years to puberty" and adults "all those beyond puberty." Only the ten commonest of the thirty-two Cooper types of pneumonia are considered. The total number of pneumococcal pneumonias was: infants 381, children 371 and adults 3,065. The ten types of pneumococci represented 63 per

cent of all pneumococcal pneumonias in infants, 78.8 per cent in children and 74.5 per cent in adults. The mortality for these ten types of pneumonia among adults was 26.9, infants 16.2 and children 4.1 per cent. In the pneumococcal pneumonias the blood was most frequently invaded in adults (23.5 per cent). The rate for infants was 6.7 and for children 4.1 per cent. In the positive blood culture cases, infants showed the highest death rate (83.3 per cent), adults 74.1 and children 25 per cent. The four important classifications of nonpneumococcal pneumonias represented 66.7 per cent of all nonpneumococcal pneumonias in infants, 84.3 in children and 76.6 per cent in adults. In these cases the death rate was 29.8 in adults, 21.2 in infants and 4.6 per cent in children. In the nonpneumococcal pneumonias, the blood was most frequently invaded in adults (16.1 per cent). In infants it was 4 per cent and for children 1.7 per cent. In the positive blood culture cases, infants showed the highest death rate (100 per cent), adults 95 per cent and children 75 per cent.

**Amphetamine Sulfate in Persistent Hiccup.**—Shaine found amphetamine sulfate to be of value in relieving two cases of persistent hiccup. In both cases it is apparent that amphetamine sulfate, perhaps through its action on smooth muscle, controlled the spastic condition responsible for the hiccup. The dose of amphetamine sulfate was from 10 to 20 mg. once or twice daily.

### Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

22: 669-818 (Nov.) 1938

Provision of Treatment for Genito-Infectious Disease in the Indigent. N. A. Nelson, Boston.—p. 669.

\*Sulfanilamide: Study of Its Effect on Bactericidal Power of Whole Blood for Gonococcus. C. S. Keefer and L. A. Rantz, Boston.—p. 679. Sulfanilamide Therapy in Hospitalized Gonorrhea. J. F. Mahoney, C. J. Van Slyke and J. D. Thayer, Stapleton, N. Y.—p. 691.

Laughlin Test as Compared to the Kahn and Modified Kolmer Serodiagnostic Tests for Syphilis. R. B. Dienst and E. S. Sanderson, Augusta, Ga.—p. 699.

Influence of Sulfanilamide on Gonococci and Gonococcal Infections. R. D. Herrold and E. Palmer, Chicago.—p. 705.

Quantitative Provocative Reactions in Normal and Syphilitic Serums Following Injection of Neosphenamine. C. W. Barnett, G. V. Kulchar and R. B. Jones, San Francisco.—p. 712.

Suggestions for Elevating Standard of Gonorrhea Clinics. M. Wishengrad, New York.—p. 717.

Absorption and Elimination of Bismuth Following Its Oral Administration to Rabbits. E. K. Stratton, San Francisco.—p. 728.

Bismuth Studies: VII. Bismuth Distribution in Dogs Following Intramuscular Injection of Single Dose of Various Bismuth Preparations. T. Sollmann and Katharine Henderson, Cleveland.—p. 739.

Extragenital Syphilis as Described in the Early Literature (1497-1624), with Special Reference to Focal Epidemics. E. L. Zimmermann, Baltimore.—p. 757.

### Sulfanilamide and Gonocidal Power of Whole Blood.

—Keefer and Rantz show that the administration of sulfanilamide by mouth in adequate amounts to patients with gonococcal infection is followed by an increase in the bactericidal power of the blood for the gonococcus. That this is due to the presence of sulfanilamide and not to the development of specific antibodies was shown by giving the drug to noninfected individuals and by adding the drug directly to whole blood of individuals with and without antibodies. The addition of the drug to serum was as effective as adding it to whole blood, showing that cells and phagocytosis were not necessary for the killing of the gonococcus in these experiments. Heating the plasma to destroy normal antibody reactions did not affect the action of sulfanilamide on the gonococcus. When the drug is discontinued, the concentration in the blood declines rapidly so that within from forty-eight to seventy-two hours most of the sulfanilamide has disappeared. The exception to this is the presence of renal insufficiency. Under these conditions the blood may continue to show large amounts of sulfanilamide for many days. When sulfanilamide is added to ascitic broth there is evidence for a bacteriostatic effect except when small numbers of organisms are used in the original inoculum. Under these circumstances the organisms fail to survive. In the treatment of gonococcal infections maximal effects can be obtained by giving 5 Gm. of sulfanilamide daily and by keeping the sulfanilamide concentration of the blood at 5 mg. per hundred cubic centimeters of blood. The presence of sulfanilamide in the blood and the synovial fluid will aid in the destruction of organisms in the joints and it will also aid in preventing the spread of organisms from a local focus, but it will not cause complete sterilization



of a local focus of infection in the genital tract in every case. Before complete recovery can take place the defense mechanism of the body must increase or retain the capacity to destroy organisms in the local focus. The administration of the drug should be continued until immune bodies have developed.

### American Journal of Tropical Medicine, Baltimore

18: 437-624 (Sept.) 1938. Partial Index

- Yellow Fever Vaccination with Cultured Virus (17D) Without Immune Serum. H. H. Smith, H. A. Penna and A. Paoliello.—p. 437.
- Beriberi or Inanition? I. Effect of Starvation, With and Without Vitamin B<sub>1</sub>. E. B. Vedder and A. B. Chinn, Washington, D. C.—p. 469.
- Id.: II. Administration of Vitamin B<sub>1</sub> to Rats Receiving Unbalanced Diets. E. B. Vedder, Washington, D. C.—p. 477.
- Vernal Vivax Activity in Persons Simultaneously Inoculated with Plasmodium Vivax and Plasmodium Falciparum. M. F. Boyd and S. F. Kitchen, Tallahassee, Fla.—p. 505.
- Deficient Homologous Immunity Following Simultaneous Inoculation with Two Strains of Plasmodium Vivax. M. F. Boyd, W. H. Kupper and C. B. Matthews, Tallahassee, Fla.—p. 521.
- Effect of Small Amounts of Quinine Administered on a Single Day on Subsequent Course of Infections with Plasmodium Vivax and Plasmodium Falciparum. M. F. Boyd and S. F. Kitchen, Tallahassee, Fla.—p. 525.
- Final Report on Use of Atabrine in Prophylaxis and Treatment of Malaria. W. N. Bispham, Baltimore.—p. 545.
- Lesions of Syphilis in American Indians. G. C. Shattuck, Boston.—p. 577.
- \*Venereal Fusospirochetosis. E. von Haam, Columbus, Ohio.—p. 595.
- Studies on Oxyuriasis: VII. Clinical Improvement Following Treatment with Single Doses of Tetrachlorethylene. W. H. Wright, J. Bozicevich and L. S. Gordon, Washington, D. C.—p. 609.

**Venereal Fusospirochetosis.**—During studies on the etiology of pudendal infections von Haam encountered progressive and destructive ulcerations of the external genitalia which originated usually, but not exclusively, in the mucous membrane and exuded a copious, purulent, hemorrhagic discharge of penetrating fetid odor. Smears from the exudate showed much necrotic cellular material with numerous pus cells and an abundant amount of fusiform bacilli, spirochetes and vibrios, the characteristic flora of Vincent's infection of the mouth. Routine bacterial cultures demonstrated only a slight participation of the common pyogenic flora in the ulcerative processes, while other venereal diseases could be excluded by careful laboratory examination. The usual local antiseptic therapy did not influence the steadily progressive character of the ulcerations, which in some cases led to extensive mutilation of the external genitalia. The characteristic presence of Vincent's flora in the discharge and the absence of other demonstrative etiologic agents seemed sufficient proof that the lesions were caused by the group of fusospirochetal organisms. Among 622 patients examined in the diagnostic laboratory for venereal diseases established at the Charity Hospital in New Orleans, thirty-seven cases of primary fusospirochetal infection of the genitalia have been recognized. The Negro race, the male sex (twenty-three cases) and the age groups between 20 and 30 years were most frequently represented in the patients suffering from the infection. Intense local pain and penetrating foul discharge were the principal clinical manifestations. Constitutional symptoms were present in twelve patients and one patient died.

### American Review of Tuberculosis, New York

38: 531-650 (Nov.) 1938. Partial Index

- Body Section Radiography with Laminagraph in Pulmonary Disease. S. Moore, St. Louis.—p. 538.
- Mediastinal and Hilar Angiography in Pulmonary Disease: Preliminary Report. I. Steinberg and G. P. Robb, New York.—p. 557.
- Bilateral Artificial Pneumothorax. B. H. Douglas, D. H. Saley and C. J. Stringer, Northville, Mich.—p. 570.
- \*End Results of Thoracoplasty. L. S. Peters and P. G. Cornish, Albuquerque, N. M.—p. 586.
- Pulmonary Emphysema in Tuberculosis. E. Korol, Lincoln, Neb.—p. 594.
- Tuberculosis of Thyroid Gland. H. W. Louria and M. R. Louria, Brooklyn.—p. 606.
- Unusual Mycobacterial Infections. G. Freeman, Chicago.—p. 612.
- Basophilic Erythrocytes in Silicosis. T. A. Neal, Detroit.—p. 629.
- \*Immunization Against Tuberculosis: Study of Essential Factors. M. I. Levine, P. Vogel and H. A. Rosenberg, New York.—p. 632.

**End Results of Thoracoplasty.**—To show how few private patients can be traced, Peters and Cornish are able to report on but seventy-eight cases out of a series of more than 300. There were forty patients on whom a complete thoracoplasty was performed, 21 per cent of whom became well (negative

sputum and cavity closed) while 54 per cent are dead. All these patients were hopelessly ill and would ultimately have died had it not been for the surgical intervention. None were able to work even part time. The others are living with positive sputum and open cavity no better than before operation and will ultimately die of tuberculosis. There were thirty-eight patients on whom a partial thoracoplasty was done, 50 per cent of whom are well (cavity closed and sputum negative) and 34 per cent are dead. The others still show positive sputum, open cavity and inability to work. They too will no doubt die of tuberculosis, but had thoracoplasty not been done all would have died of their disease. The indications for thoracoplasty are about the same as for pneumothorax. These end results, as well as others reported in the literature, prove that all patients who must otherwise die of their tuberculosis should be given the benefit of thoracoplasty if they offer a fighting chance for recovery. To do less is to sacrifice lives that might otherwise be saved. All those reported well have been so for from two to fifteen years.

**Immunization Against Tuberculosis.**—During the last eleven years a study on the efficacy of BCG vaccination against tuberculosis in children has been carried on in New York City by the Bureau of Laboratories of the Department of Health. Levine and his colleagues report on the methods used up to April 1, 1937, during which time 1,830 children of tuberculous families have been followed, of which 880 were vaccinated and 950 served as controls. In the course of these eleven years of study the importance of selecting adequate controls has been emphasized repeatedly. At the outset of the study an attempt was made to control the experiment by dividing the children into two equal groups, those vaccinated and those not vaccinated. This procedure (usually the children of cooperative parents) was followed from 1926 to Jan. 1, 1933. In all 955 children were studied, 435 of whom were vaccinated, when the procedure of selection was changed so that alternate children were vaccinated and the others served as controls. Under this selection 744 children were observed from Jan. 1, 1933, to Sept. 1, 1936, 383 being vaccinated and 361 held as controls. The results of BCG vaccination before alternate selection was sixteen deaths in the control and three deaths in the vaccinated group. The results of BCG vaccination after alternate selection was instituted was four deaths in the control and six in the vaccinated group. It would seem, therefore, that the manner of selecting cases for vaccination or as controls exerted a marked influence on the final results obtained. A complete study of the participating factors is to be the basis of a forthcoming article.

### Archives of Pathology, Chicago

26: 923-1092 (Nov.) 1938

- \*Carbon Tetrachloride Poisoning: Study of Stages of Hepatic Damage and Repair in Man. T. M. Peery, Washington, D. C.—p. 923.
- Calcification of Hyaline Cartilage in Man. B. Falconer, Stockholm, Sweden.—p. 942.
- \*Tissue Reactions to Natural Oils and Fractions Thereof. G. M. Hass, Boston.—p. 956.
- Effect of Primary Pulmonary Tuberculous Lesion (BCG) on Experimental Pulmonary Tuberculosis in Rabbits. B. J. Clawson, Minneapolis.—p. 966.
- Morphologic Study of Reactivity of Mouse Sarcoma 180 to Bacterial Filtrates. I. E. Gerber and Alice Ida Bernheim, New York.—p. 971.
- Effect of Sympathectomy on Vasa Vasorum of the Rat. J. Q. Griffith Jr., C. J. Zinn and B. I. Comroe, with technical assistance of R. Campbell, Philadelphia.—p. 984.
- Experimental Gastric Ulcer (Pitressin Episodes). A. J. Nedzel, Chicago.—p. 988.
- Pathologic Observations on Adenomatous Lesion of Stomach in Mice of Strain I. H. L. Stewart and H. B. Andervont, Boston.—p. 1009.
- Cirrhosis of Liver in Rabbits with Continued Chloroform Poisoning and with Associated Syphilitic Infection. H. W. Ferris, New York.—p. 1023.
- Hyperparathyroidism Secondary to Experimental Renal Insufficiency. W. J. Highman Jr. and B. Hamilton, Chicago.—p. 1029.
- Case of Primary Reticulum Cell Sarcoma of the Brain: Relationship of Microglia Cells to Histiocytes. C. L. Yuile, Boston.—p. 1036.
- Erythroblasts in Chorionic Blood Vessels of Human Embryos. B. Halpert and J. Stasney, New Orleans.—p. 1045.
- Metastatic Calcification in a Case of Carcinoma of the Breast. J. W. Egoville, Philadelphia.—p. 1047.

**Carbon Tetrachloride Poisoning.**—Peery cites three cases of accidental poisoning by carbon tetrachloride in man that have been studied clinically and at necropsy. The deaths resulted from ingestion of a "roach poison" containing a mixture of

carbon tetrachloride and ethylene dichloride, mistaken for an intoxicant. One victim died about eight hours after taking the drug and showed no definite lesions at necropsy. The second died about sixty-eight hours after ingesting the poison and at necropsy acute necrosis of the liver was observed. The third patient died 150 hours after poisoning and at necropsy active regeneration of lost liver cells was seen.

**Tissue Reactions to Natural Oils.**—In order to determine the reactions of the tissues of experimental animals to oils, Hass injected olive oil and cod liver oil subcutaneously, intramuscularly and intraperitoneally in doses of 0.5, 0.25, 0.1 and 0.05 cc. Old and young animals were used. The tissues were examined at intervals of one, two and three weeks after the injection of each oil. Olive oil persists in an unchanged state in the intercellular medium of the subcutaneous tissues over a period of three weeks. During the same interval cod liver oil is partly transformed into an amorphous homogeneous semisolid material. A part of this material is insoluble in water, alcohol and xylene. Some of the insoluble substance is acid fast. The study of the various fractions of the hydrolyzed oils and the methyl esters of the acid products of hydrolysis shows that the amorphous semisolid material is formed in the intercellular region only in the presence of unsaturated fatty acids or methyl esters of unsaturated fatty acids. An increase in the amount of this material is correlated with an increase in the average unsaturation of the fractions employed. An increase in the intensity of the inflammatory response is associated with an increase in the average unsaturation of the fraction introduced into the tissue spaces. An infiltration with eosinophils is prominent in the zones of reaction to several of the unsaturated fractions in contrast with the relative infrequency of these cells in the zones of reaction to saturated compounds. The numerical distribution of multinucleated giant cells in the regions of response to the unsaturated liquid compounds indicates that the amorphous semisolid material derived from these compounds is the only effective stimulus to giant cell formation. The liquid methyl esters of the saturated acids, in contrast to the glyceryl esters, are rapidly hydrolyzed in the intercellular environment.

#### Arkansas Medical Society Journal, Fort Smith

35: 105-122 (Nov.) 1938

Diagnosis of Acute Abdomen. G. E. Cannon, Hope.—p. 105.  
Hypotension and Its Significance. J. M. Samuel, Little Rock.—p. 108.

#### Bulletin New York Academy of Medicine, New York

14: 653-710 (Nov.) 1938

\*Chemistry and Biology of Male Sex Hormones. F. C. Koch, Chicago.—p. 655.  
The Management of Hypertension. H. J. Stewart, New York.—p. 681.

**Testis Hormones.**—Koch points out that at present six androgens have been found in nature and that four of them have been isolated from human urine. Only androsterone and dehydro-androsterone have been separated from the urine of normal men. Whether all the androgenic activity in these urines resides in these compounds or whether others contribute remains to be determined. Although normal women also excrete large amounts of androgenic material, its exact nature has not been determined. Thus far, pure androgen has not been separated from the urine of normal nonpregnant women. However, in the pregnant woman epiallopregnanolone-3,20 has been separated from the urine as one of the androgens. In pathologic urines there undoubtedly are varying amounts of androsterone and pregnanetriol-3,17,20 in addition to androsterone, dehydro-androsterone and many other possible compounds of androgenic character. The normal type of androgen may be increased in concentration in pathologic conditions. In view of the possibilities of complex mixtures existing in various urines in various proportions it is probable that future advances in the quantitative studies on urine will depend to a large extent on the ability to differentiate quantitatively between the different androgens. However, for the present one must be content with the estimation of the total androgenic activity in tissue, body fluids and excretions in attempts to correlate the quantitative information with various endocrine disturbances possibly involving the gonads.

#### Delaware State Medical Journal, Wilmington

10: 205-222 (Oct.) 1938

The Medical Approach to Sex Instruction in Schools of Delaware. C. J. Prickett, Smyrna.—p. 205.  
Industrial Law and the Medical Profession. J. B. McManus, Wilmington.—p. 209.  
Treatment of Pneumonia. J. J. Cassidy, Wilmington.—p. 213.

#### Endocrinology, Los Angeles

23: 535-680 (Nov.) 1938

Oral Administration of Hormone Proteins: Thyroid Protein and Insulin. Hildegard Wilson, T. S. Sappington and W. T. Salter, Boston.—p. 535.  
Effect of Hyperthyroidism on Growth and Chemical Composition of Bone. Evelyn E. Smith and F. C. McLean, Chicago.—p. 546.  
Relation of Environmental Temperature to Action of Thyroxine. L. H. Schmidt and Ida Genter Schmidt, Cincinnati.—p. 553.  
Variations in Structure of Adrenals and Thyroids Produced by Thyroxine and High Environmental Temperatures. Ida Genter Schmidt and L. H. Schmidt, Cincinnati.—p. 559.  
\*Syndrome of Infantilism, Congenital Webbed Neck and Cubitus Valgus. H. H. Turner, Oklahoma City.—p. 566.  
Influence of Avitaminoses on Weights of Endocrine Glands. B. Sure, Fayetteville, Ark.—p. 575.  
Modified and Improved Method for Preparation of Thymus Extract. A. Steinberg, Philadelphia.—p. 581.  
Certain Iodine-Reducing Substances of Thymus Extract: Biologic Considerations. L. G. Rowntree, A. Steinberg, N. H. Einhorn and N. K. Schaffer, Philadelphia.—p. 584.  
Id.: Chemical Analysis of Extract. N. K. Schaffer, W. M. Ziegler and L. G. Rowntree, Philadelphia.—p. 593.  
\*Effect of Anterior Pituitary Sex Fraction on Development of Human Uterus. S. A. Payne and E. K. Shelton, Los Angeles.—p. 598.  
Hyaline Change in Basophil Cells of Pituitary Body Not Associated with Basophilism. A. D. Ecker, Rochester, Minn.—p. 609.  
Comparative Effects of Light Stimulation and Administration of Gonadotropic Hormones on Female Sparrows. G. M. Riley and E. Witschi, Iowa City.—p. 618.  
Subclinical Adrenogenital Syndrome. S. J. Glass and H. C. Bergman, Los Angeles.—p. 625.  
Insulin Insensitivity: Its Possible Relation to Pituitary Gland. G. Flaum, New York.—p. 630.  
Juvenile Adiposogenital Dystrophy: Neurologic and Psychopathologic Aspects: Results of Organotherapy and Psychotherapy. B. Mittelman, New York.—p. 637.

**Infantilism, Webbed Neck and Cubitus Valgus.**—Turner believes that infantilism, webbing of the skin of the neck and deformity of the elbow (cubitus valgus) occurring in the same person is unusual and to his knowledge has not been reported previously. The individual signs are perhaps not uncommon. The seven female patients forming the basis of the author's report cannot be classified under the syndrome of Klippel-Feil, Sprengel's deformity or cervical Pott's disease, as the shortening of the neck is merely apparent, due to the webbing, and not real. There is no absence or fusion of the cervical spine in any of these patients. There is some lowering of the hairline on the back of the neck, but no marked limitation of motion. Torticollis, mirror movements, facial asymmetry and other signs and symptoms, such as difficulty in breathing or swallowing, and shortness of breath, are not present. There is no mental retardation. Deformity of the elbow, consisting of an increase in the carrying angle, or cubitus valgus, is constantly present. All of the author's patients present osseous and sexual retardation similar to that associated with hypo-antuitarism, or the Lorain-Levi type of dwarfism. The blood and urine of these patients were entirely within normal limits. Roentgenograms of the skull, cervical spine, elbow, wrist and pelvis revealed no abnormalities with the exception of demineralization and evidence of delayed union of the epiphyses in six patients. Treatment with pituitary growth hormones has been unsatisfactory. There was definite genital development following the administration of the anterior pituitary gonadotropic substance in the two patients treated.

**Gonadotropic Substance and Development of Human Uterus.**—Payne and Shelton encountered ten women with small uteri (a depth of less than 2 inches) during a period of twelve months. All had some menstrual disturbance when first seen. A gonadotropic extract derived from the anterior pituitary glands of either hogs or sheep was used. Secondary menstrual disturbances occurred in three women of the group: following an acute infection, a change in climate and environment and after a severe nervous shock. The endometrium obtained by biopsy at the beginning of treatment was atrophic

in all patients. Since there was a response to treatment in all but two of the women, it became apparent to the authors that they were dealing not only with a problem of uterine hypoplasia but also with gonadal insufficiency. In seven of the eight women who responded to treatment there was improvement in menstruation and the endometrium became more normal following injections of the gonadotropic substance. Following these injections the endometrium changed to a secretory type in four patients and one other woman became pregnant, suggesting that anterior lobe extracts may have an influence on ovulation. Uterine growth occurred in three patients, the uterine depth increased from  $1\frac{1}{4}$  to  $3\frac{1}{4}$ ,  $1\frac{3}{8}$  to 3 and  $1\frac{1}{2}$  to  $2\frac{1}{4}$  inches respectively in each woman. It is impossible to draw definite conclusions, but it appears that the anterior pituitary elaborates a substance which stimulates the gonads, including an influence on ovulation and in some cases on uterine growth. Uterine development follows its administration.

### Illinois Medical Journal, Chicago

74: 385-476 (Nov.) 1938

- The Position of the American Medical Association. I. Abell, Louisville, Ky.—p. 407.  
The Educational Committee: Its Origin and Work. J. H. Hutton, Chicago.—p. 411.  
Subcutaneous Injuries of the Abdomen. F. Christopher, Evanston.—p. 415.  
Injuries to the Right Upper Abdominal Quadrant. P. H. Kreuscher, Chicago.—p. 419.  
Ruptured Spleen. C. C. Guy, Chicago.—p. 423.  
Mosquito Control in Illinois as a Public Health Measure. S. S. Fuller, Riverside.—p. 428.  
Symptom Complex of Visceral-Spinal Pain. E. L. Compere, Chicago.—p. 434.  
Pneumonectomy for Bronchogenic Carcinoma of the Lung: Report of Successful Case Sixteen Months After Operation. W. E. Adams, Chicago.—p. 442.  
\*Milk Sickness. G. H. Gowen, Champaign.—p. 447.  
Some Practical Suggestions in Control of Venereal Diseases. A. J. Levy, Chicago.—p. 452.  
Amaurotic Family Idiocy (Juvenile Form): Report of Two Cases Occurring in the Same Family. H. B. FitzJerrrell and B. B. Neuchiller, Dixon.—p. 456.  
Stab Wounds of the Cervical Spinal Cord. K. L. Vehe and R. E. Lyons, Chicago.—p. 461.  
Consideration of Some Practical Points in the Management of Inflammatory Diseases of Uveal Tract. G. L. Porter, Urbana.—p. 463.  
Sulfanilamide: Its Use in General Practice. A. F. Goodyear, Decatur.—p. 469.

**Milk Sickness.**—Gowen presents a review of the literature on milk sickness or "trembles." This condition is due to trematol, one of the toxic constituents of white snakeroot (*Eupatorium urticaefolium*). Milk sickness in man and "trembles" in domestic animals are identical. Animals acquire the disease by eating white snakeroot. Man acquires the disease by consuming milk or milk products from animals that have been eating the plant. Pasteurization does not destroy the poisonous properties. Trembles appear only in pastured animals. In every outbreak investigated by the author the animals had been turned into a wooded area, owing to lack of any other means of nourishment. The symptoms of milk sickness most commonly described and seemingly characteristic in order of occurrence are weakness or prostration, pernicious vomiting, severe constipation and epigastric pain. The temperature is characteristically normal or subnormal. Muscular pains are common. There is marked thirst, the urine is scanty, frequently acetone is found, and the breath has a distinct odor of acetone. Flushed cheeks and undue redness of the lips and tongue are not infrequent. Swelling of the tongue is commonly experienced by the patient. In fatal cases, coma and convulsions precede death. In patients who recover, weakness persists for days, weeks or even months, depending on the initial severity of the illness. Seemingly recovered patients may relapse if undue physical exertion is practiced too soon. In the author's twenty-one patients (two died) there was a direct relationship between the quantity of milk or milk products consumed and the severity of the disease. In general, treatment consists of saline purgation, fluids, alkalis by mouth, dextrose intravenously and enemas. The old remedy of brandy and honey finds some basis in the statement of Hardin, who says:

"The administration of alcohol causes an ester of trematol to be formed which is less toxic. If the patient becomes overheated before the ester is excreted, a hydrolysis of the ester occurs, liberating the poison."

### Journal Industrial Hygiene & Toxicology, Baltimore

20: 497-534 (Oct.) 1938

- The Heated Thermometer Anemometer. C. P. Yaglou, Boston.—p. 497.  
Use of New Equipment and Helium Gas in a World Record Dive. E. End, Milwaukee.—p. 511.  
Can Lead Poisoning Cause Gastric-Duodenal Ulcers? C. Csépai, Budapest, Hungary.—p. 521.  
Methemoglobinemia and Its Measurement. D. O. Hamblin and A. F. Mangelsdorff, Bound Brook, N. J.—p. 523.

### Journal of Investigative Dermatology, Baltimore

1: 313-398 (Oct.) 1938

- Parasitic Skin Diseases of Domesticated Animals and Their Importance to Dermatologists: A Review. H. M. Martin.—p. 313.  
Xanthomatosis: III. Cutaneous Xanthoma, Especially in Relation to Disease of Liver. H. Montgomery, Rochester, Minn.—p. 325.  
Studies in Experimental Congenital Syphilis and Transference of Immunity from Immune Syphilitic Female Rabbits to Their Offspring. J. E. Kemp and Elsie Mae Fitzgerald, Chicago.—p. 353.  
Skin Test in Lymphogranuloma Inguinale: Brief Review and Discussion of Some Possible Causes of Error. W. Frei, New York.—p. 367.  
\*Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi: Historical Review, Nomenclature and Theories Relative to the Nature of the Disease, with Experimental Studies of Two Cases. S. W. Becker and H. W. Thatcher, Chicago.—p. 379.

**Multiple Idiopathic Hemorrhagic Sarcoma.**—Becker and Thatcher discuss the various designations and theories of the origin and etiology of Kaposi's sarcoma. The disease is seen predominantly in Italians and Jews. Incidence late in life with the peak at 70 years suggests neoplastic rather than infectious origin. In most cases the lesions have their onset on the lower extremities. Two cases are presented, one of which ended fatally, with true sarcoma formation. The injection of material from a benign lesion into a patient and a rabbit did not cause the formation of a tumor. The most logical explanation of Kaposi's sarcoma is that it is a multicentric benign neoplasm originating in the perithelial tissue from embryonic mesenchymal cells (lymphocytoid cells of Marchand), which results in a type of cell growth unique for the disease. After a period of years, the cells may undergo malignant degeneration, producing true sarcoma, resulting in metastasis and death. Metastasis by way of the lymphatics in contrast to hematogenous metastasis of most nonlymphocytic sarcomas may be construed as evidence of the lymphocytoid origin of the disease.

### Journal-Lancet, Minneapolis

58: 465-504 (Nov.) 1938

- Diabetes Mellitus and Protamine Zinc Insulin. A. R. Foss, Missoula, Mont.—p. 465.  
Management of Squint. G. M. Constans, Bismarck, N. D.—p. 470.  
Student Cooperation in Tuberculosis Control. K. Emerson, New York.—p. 476.  
\*Chronic Recurring Sciatic Pain Due to Protruded Intervertebral Disks. J. G. Love, A. W. Adson and W. M. Craig, Rochester, Minn.—p. 479.  
Practical Points in Interpretation of Allergy Skin Tests. A. V. Stoesser and Ruth Greenberg, Minneapolis.—p. 482.  
Infant Feeding. F. W. Schlutz, Chicago.—p. 485.  
Vitamin D Deficiency in Infancy and Childhood. P. H. Woutat, Grand Forks, N. D.—p. 493.  
Prevalence of Positive Wassermann Reaction, with Special Reference to Railroad Employees. W. Hiemstra, Missoula, Mont.—p. 495.

**Sciatic Pain from Protruded Intervertebral Disks.**—Love and his colleagues believe that many persons who are suffering from persistent or recurrent attacks of sciatic pain are harboring a protruded intervertebral disk, removal of which will result in dramatic relief of the symptoms. Intervertebral disks may be protruded as a result of an accident or of unusual stress or strain, such as lifting a heavy object. Although any one of the disks may be protruded, those most commonly subjected to this accident are in the lumbar region. The fourth and fifth (lumbosacral) disks are most frequently the cause of the patient's disability. The chief symptoms in cases of protrusion of intervertebral disks are root pain. Since the protrusion most often occurs in the lumbar region, the chief complaint is of pain low in the back and of sciatic pain, usually unilateral. On examination, Lasègue's test (raising the

straight leg) is usually positive and often the achilles tendon reflex on the involved side is diminished or absent. Because of the cases in which values for total protein in the cerebrospinal fluid are normal or low, the authors employ a reversed Queckenstedt test, which is helpful in the diagnosis of lumbar protrusions. This test is based on essentially the same principles as the usual Queckenstedt test, except that the increase in intraspinal pressure in the caudal sac is produced by the extradural injection of a 1 per cent solution of procaine hydrochloride whereas in the Queckenstedt test the pressure comes from within, when the return vascular circulation (internal jugular veins) is obstructed. One of the most important results of this test is the patient's reaction to compression of the cauda equina by the extradural solution. In case of a lesion involving one or more roots of the cauda equina, compression of the caudal sac produces excruciating pain in the involved root. If the value for total protein is normal or low, the reversed Queckenstedt test should be positive before the diagnosis of protruded disk is made. The diagnosis is confirmed and the protruded disk is identified by x-ray examination, after subarachnoid injection of 5 cc. of iodized oil between the spinous processes of the third and fourth lumbar vertebrae. If, on x-ray examination, a persistent defect characteristic of protruded disk is noted and if a lesion at that level could account for the patient's pain, surgical removal of the protruded portion of the disk is indicated. The operative procedure consists of laminectomy and removal, either extradural or transdural, of the protruded portion of the disk. The iodized oil is removed at the time of laminectomy. Fixation of the spine is not necessary. In more than 150 cases the authors have not found it necessary or advisable to perform fusion. The patients are treated postoperatively as if they had undergone simple laminectomy for tumors of the spinal cord. They are kept in bed twelve days and are allowed to leave the hospital on the fourteenth day and to return to their homes three weeks following operation. They are advised to refrain from heavy lifting and straining for at least three months.

### Journal of Nervous and Mental Disease, New York

88: 569-732 (Nov.) 1938

- Olivopontocerebellar Atrophy and Unilateral Involvement of Cranial Nerve Nuclei. C. Davison and I. S. Wechsler, New York.—p. 569.  
Psychosurgery: Effect on Certain Mental Symptoms of Surgical Interruption of Pathways in Frontal Lobe. J. W. Watts and W. Freeman, Washington, D. C.—p. 589.  
Pathology of Huntington's Chorea. T. T. Stone and E. I. Falstein, Chicago.—p. 602.  
Psychosomatic Relationships in Pruriginous Lesions. H. Kelman and H. Field, New York.—p. 627.  
Psychologic Considerations of Insulin Treatment in Schizophrenia. L. L. Orenstein and P. Schilder, New York.—p. 644.

### Journal of Pharmacology & Exper. Therap., Baltimore

64: 131-242 (Oct.) 1938

- Experiments with an "Antineurotic" Material Prepared from Liver. H. M. Barrett, D. L. MacLean and E. W. McHenry, Toronto.—p. 131.  
Effect of Alarm Reaction on Absorption of Toxic Substances from Gastrointestinal Tract. H. Selye, Montreal.—p. 138.  
Trypanocidal Activity and Arsenic Content of Cerebrospinal Fluid After Administration of Arsenic Compounds: II. F. Hawking, T. J. Hennelly and W. T. Wales, with assistance of W. Chinnick; appendix by R. E. Barrett, Cardiff, Wales.—p. 146.  
Spirocheticidal Action of Arsphenamines on Spirochaeta Pallida in Vitro. H. Eagle, Baltimore.—p. 164.  
Action of Sympathomimetic Amines on Heart-Lung Preparation. J. M. Crismon and M. L. Tainter, San Francisco.—p. 190.  
Hydrolysis of Homatropine and Atropine by Various Tissues. F. Bernheim and Mary L. C. Bernheim, Durham, N. C.—p. 209.  
Effect of Autonomic Hormones on Thyrotoxic Heart. B. Wise and H. E. Hoff, New Haven, Conn.—p. 217.  
\*Anesthetic Effects of Chlorine Derivatives of Cyclopropane. V. E. Henderson, Toronto.—p. 225.  
Studies on Cholinesterase Activity: I. Manometric Method of Assaying Cholinesterase Action. M. Rinkel and M. Pijoan, Boston.—p. 228.  
Studies of Morphine, Codeine and Their Derivatives: XIII. Clinical Study of Comparative Effects of Dihydroisocodeine and Codeine. L. F. Davenport, Boston.—p. 236.

**Anesthetic Effects of Cyclopropane.**—By experimenting on a rabbit and cats, Henderson found that both monochlorocyclopropane and dichlorocyclopropane are not suitable for anesthesia, as they cause irritation of the lungs. Cats forced to full saturation with cyclopropane take up large quantities

of gas, certainly more than 100 cc. per kilogram, and in some cases at least 150; similarly animals receiving methyl cyclopropane absorbed, under similar conditions, equal amounts in spite of its greater anesthetic potency. The evidence from the chlorinated cyclo compounds strongly suggests that substituted cyclopropanes are unstable in the body.

### Journal of Urology, Baltimore

40: 467-550 (Oct.) 1938

- Tumor of Medulla of Adrenal (Adrenal Pheochromocytoma) with Removal and Relief of Paroxysmal Hypertension. D. W. MacKenzie and D. McEachern, Montreal.—p. 467.  
Renal Tumors: Review of 130 Cases. H. M. Soloway, Chicago.—p. 477.  
Perirenal Fibrosarcoma. H. H. Howard and H. I. Suby, Boston.—p. 491.  
Pelvic Kidney and Renal Vessels in a Newborn Child. G. A. Boylston and B. J. Anson, Chicago.—p. 502.  
Spontaneous Rupture of Tuberculous Bladder. T. E. Wyatt and H. L. Douglass, Nashville, Tenn.—p. 506.  
Why Are Abnormal Cystometrograms Obtained in Normal Patients? M. L. Boyd and W. A. Smith, Atlanta, Ga.—p. 513.  
Dilatation of Contracted Bladder: New Instrument. W. M. Kearns, Milwaukee.—p. 519.  
Carcinoma of Prostate with Metastasis in Testis. J. H. Semans, Baltimore.—p. 524.  
Metastases from Occult Carcinoma of the Prostate. O. S. Culp, Baltimore.—p. 530.  
Testicular Tumors in Dogs. C. F. Schlotthauer, J. R. McDonald and J. L. Bollman, Rochester, Minn.—p. 539.

### Kansas Medical Society Journal, Topeka

39: 413-456 (Oct.) 1938

- Hoarseness. H. W. Powers, Topeka.—p. 413.  
Pyogenic Osteomyelitis of the Pelvis: Analysis and Discussion of a Single Case. R. C. Jeffries, Atchison.—p. 417.  
Essential Hypertension and Cardiovascular Disease. A. Arkin, Chicago.—p. 418.  
Diagnostic Errors in the Field of Internal Medicine. J. M. Porter, Concordia.—p. 420.

### Laryngoscope, St. Louis

48: 615-698 (Sept.) 1938. Partial Index

- The Management of Cancer of the Nasal Sinuses. M. C. Myerson, New York.—p. 615.  
Chronic Frontal Sinusitis: A New Endonasal Surgical Approach. F. E. Stone and M. Berger, Brooklyn.—p. 626.  
Treatment of Laryngeal Carcinoma. R. Kramer, New York.—p. 645.  
The Art of Good Tone Production, with Some Helpful Suggestions. H. A. Schatz, Philadelphia.—p. 656.  
Tetanus Associated with Acute Otitis Media; Probable Atrium Tetanus: Report of Two Cases. P. S. Stout, Philadelphia.—p. 682.

48: 699-764 (Oct.) 1938

- \*Use of Estrogenic Substances in Atrophic Rhinitis. I. H. Blaisdell, Boston.—p. 699.  
Concussion Sound Waves from Large Guns in Action: Author's Abstract. D. C. Miller, Cleveland.—p. 720.  
Diseases of Maxillary Sinus and Their Relationship to Oral Cavity. J. M. Loré, New York.—p. 724.  
Modification of Semilunar Ganglion Approach Used in Surgery of Petrous Pyramid. M. F. Jones, New York.—p. 738.  
Sarcoma of Larynx. I. Arons, New York.—p. 745.  
Tuberculous Tonsillitis: Clinical-Pathologic Study Based on 782 Tonsillectomies. J. H. Ahronheim, Jackson, Mich.—p. 749.  
The Crooked Nose. A. A. Cinelli, New York.—p. 760.

**Estrogen in Atrophic Rhinitis.**—Blaisdell states that estrogenic substances were first used in cases of atrophic rhinitis in the outpatient department of the Eye and Ear Infirmary on Aug. 1, 1937. A series of sixty cases is presented, divided into two groups; group 1 consists of patients with an onset (true atrophic rhinitis) before 20 years of age and group 2 is made up of patients with onset (secondary atrophic rhinitis) of symptoms after 20 years of age. There was clinical improvement, as shown by diminution of crusts and odor in 86.4 per cent of the patients in group 1 and improvement of all patients in group 2. Because of its wide variety of effects on the body, aside from its function as a sex hormone, estrogen, properly used, is one of the greatest weapons for combating diseases and physiologic conditions which heretofore have been obscure. Besides acting as a hormone estrogen acts also like a drug and its action is farther reaching than insulin, more powerful than epinephrine and more spectacular than ergot. As the study of this substance progresses, its exact place in the armamentarium of the otolaryngologist will undoubtedly be found. The relationship

between menstrual abnormalities and atrophic rhinitis should be undertaken by a gynecologist. The exact mechanism by which estrogen acts on the nose is not known and the extent of changes in the mucosa, as well as the permanence of the improvement clinically, can be determined only after years of carefully studying these cases.

### Nebraska State Medical Journal, Lincoln

23: 401-440 (Nov.) 1938

- Anterior Pituitary-Gonad Relationship in the Female with Clinical Application. A. A. Werner, St. Louis.—p. 401.  
Hospital Insurance. C. C. Johnson, Lincoln.—p. 404.  
Specificity of Methods for Determining Concentration of Ethyl Alcohol in Body Fluids with Specific Reference to the Heise Method. D. F. Bavis and M. F. Arnholt, Lincoln.—p. 407.  
Further Standardization After Experience with Injection Treatment of Hernia. L. E. Hanisch, Omaha.—p. 413.  
Analysis of 186 Consecutive Ambulatory Cases of Heart Disease. E. Thompson, Omaha.—p. 415.  
Pneumatic Lift for Gallbladder and Kidney Operations. H. S. Andrews and B. B. Sutton, Minden.—p. 419.  
Bone Marrow Biopsy. J. P. Tollman, Omaha.—p. 421.  
Socialized Medicine in Sweden. P. Findley, Omaha.—p. 425.

### New England Journal of Medicine, Boston

219: 635-684 (Oct. 27) 1938

- Reported Gonorrhea and Syphilis in Massachusetts, 1930-1937. E. B. Howard, Boston.—p. 639.  
Opportunity for Modern Treatment of Lobar Pneumonia in General Practice. H. D. Levine, Bristol, N. H.—p. 644.  
Cold as a Standard Stimulus of Blood Pressure: Study of Normal and Hypertensive Subjects. D. Ayman and A. D. Goldshine, Boston.—p. 650.  
Human Autonomic Pharmacology: XIX. Effect of Mecholyl, Prostigmine, Benzedrine Sulfate and Atropine on Urinary Tract: Urographic Studies. J. Loman, B. Greenberg and A. Myerson, Boston.—p. 655.  
Activation of Peritoneal Mechanism of Defense. H. L. Johnson, Boston.—p. 661.

### New York State Journal of Medicine, New York

38: 1369-1426 (Nov. 1) 1938

- \*Type I Pneumococcus Pneumonia: Observations from Study of 2,000 Cases Treated with Specific Serum. E. S. Rogers and Marjorie E. Gooch, Albany.—p. 1369.  
Syphilis: Chance of Acquisition and Frequency of Its Disastrous Course. R. A. Vonderlehr and Lida J. Usilton, Washington, D. C.—p. 1376.  
Serodiagnosis of Infectious Disease. A. B. Wadsworth, Albany.—p. 1383.  
Fractures in the Small Hospital, with Observations on Common Sources of Error and Fundamentals and Psychology of Treatment. R. F. Sengstacken, Suffern.—p. 1387.  
Thrombocytopenic Purpura: Nonsurgical Treatment. H. M. Greenwald, Brooklyn.—p. 1391.  
Some Toxic Manifestations Following Use of Sulfanilamide. D. Greenberg, New York.—p. 1394.  
Spontaneous Rupture of Splenic Artery. A. Segal, Brooklyn.—p. 1396.  
Retrograde Intussusception of Cecum into Ileum. E. S. Goodyear, Kingston.—p. 1397.  
Slit Lamp Principle: Its Use as Simple Aid to Inspection in Physical Diagnosis. N. E. Reich, Brooklyn.—p. 1398.  
Contact Implantation of Cancer: Carcinoma of Lower and Upper Lips. H. Charache, Brooklyn.—p. 1400.

**Type I Pneumococcus Pneumonia.**—During a period of twenty-five months 2,293 cases of type I pneumococcus pneumonia occurred in New York State exclusive of New York City. Rogers and Gooch discuss the 2,027 cases that were treated with concentrated type I antipneumococcus horse serum. Age had a direct influence on prognosis in the patients treated with serum as well as those not treated with it. Sex apparently influences morbidity but not mortality, save through its relationship to pregnancy. The data suggest that pregnancy may prove to be a factor predisposing to pneumonia and that the last four months of pregnancy most seriously influence the prognosis. The seriousness of bacteremia as reported by many other observers has been corroborated. The mortality rises in direct relation to the duration of the disease at the time treatment is started. Among 544 patients treated on or before the fourth day of illness the fatality rate was 15.8 per cent, as contrasted with 33.9 per cent for 183 patients receiving treatment later than on the fourth day of illness. Of the 544 patients, 251 received less than 100,000 units of serum and 17.5 per cent of them died; 293 received 100,000 units or more and 14.3 per cent of them died. This does not offer impressive evidence in favor of large dosage. However, if the group of 293 patients is further analyzed it is found that only sixty-

six of them received what might be termed "intensive" treatment, that is to say received all their serum within a period of twenty-four hours. Of these sixty-six patients only 6.1 per cent died, while of the 227 patients who received a similar amount of serum over more than twenty-four hours, 16.7 per cent died. The use of type I serum in the treatment of improperly typed cases, untyped cases or cases of heterologous types is discouraged. Of 129 such reports (not included in the 2,027 patients in the present series) the crude case fatality rate was 28.6 per cent.

### Northwest Medicine, Seattle

37: 307-342 (Oct.) 1938

- Urgent Medical Problems. J. R. Morrison, Bellingham, Wash.—p. 312.  
Principles Which Should Govern the Therapeutic Use of Sulfanilamide. E. E. Osgood, Portland, Ore.—p. 314.  
Gastrectomy for Gastroduodenal Ulcer. E. C. Moore, Los Angeles.—p. 318.  
Gas Distention of the Appendix in Acute Appendicitis: Case Report. B. N. Wade, Portland, Ore.—p. 323.  
Treatment of Threatened and Habitual Abortion: Report of Two Cases. W. R. Frazier, Portland, Ore.—p. 324.  
Symptoms of Early Malignancy of Upper Air Passages. I. E. Gaston, Portland, Ore.—p. 326.

### Philippine Islands Med. Association Journal, Manila

18: 549-616 (Sept.) 1938

- Tuberculosis: A Public Health Problem in the Philippines Which Requires Development of Balanced National Tuberculosis Program. S. A. Francisco, Manila.—p. 549.  
Ectopic Pregnancy. H. Acosta-Sison and J. S. Galang, Manila.—p. 557.  
Multiple Serositis: Report of Case. A. B. M. Sison, Manila.—p. 565.

### Psychoanalytic Quarterly, Albany, N. Y.

7: 299-420 (July) 1938

- Psychoanalysis Comes of Age. F. Alexander, Chicago.—p. 299.  
Folie à Deux. Helene Deutsch, Boston.—p. 307.  
Akinesia After Ventriculography: Contribution to Ego Psychology and the Problem of Sleep. M. Grotjahn and T. M. French, Chicago.—p. 319.  
Telepathic Sensitiveness as a Neurotic Symptom. L. J. Saul, Chicago.—p. 329.  
Incidental Observations on Pruritus Ani. L. J. Saul, Chicago.—p. 336.  
Incidence and Character of Masturbation Threats in a Group of Problem Children. Mabel Hushka, New York.—p. 338.  
A Paranoid Mechanism in Male Overt Homosexuality. L. N. Bollmeier, Hot Springs, Ark.—p. 357.  
The Psychogenesis of a Fatal Organic Disease. B. Berliner, San Francisco.—p. 368.

### Southern Medical Journal, Birmingham, Ala.

31: 1117-1218 (Nov.) 1938

- Cysts of the Kidney. E. R. Whitmore, Washington, D. C.—p. 1117.  
Wilms' Tumors. G. W. Reagan, Little Rock, Ark.—p. 1129.  
Congenital Valves of Posterior Urethra: Report of Case Associated with Spina Bifida Occulta and Vesical Diverticulum. Emma S. Moss and J. R. Schenken, New Orleans.—p. 1134.  
\*Acute Streptococcal Lung Abscess Treated with Sulfanilamide: Case Report. F. B. Murphy Jr. and J. M. Frere, Chattanooga, Tenn.—p. 1136.  
Treatment of Skin Cancer. E. C. Fox, Dallas, Texas.—p. 1139.  
Evolution of Radiation Therapy for Carcinoma of Cervix Uteri, with Special Reference to Methods Used at Roper Hospital. B. Kalayjian and H. Rudisill Jr., Charleston, S. C.—p. 1143.  
Diagnostic Bronchoscopy. J. S. Agar, Little Rock, Ark.—p. 1150.  
Treatment of Pellagra with Nicotinic Acid: Observations in Forty-Five Cases. V. P. Sydenstricker, H. L. Schmidt Jr., M. C. Fulton, J. S. New and L. E. Geeslin, Augusta, Ga.—p. 1155.  
\*Further Observations on Effect of 2,6-Dimethyl Dinicotinic Acid and Dinicotinic Acid on Pellagrins in Relapse and on Normal Persons. Sue Potter Vilter, W. B. Bean and T. D. Spies, Cincinnati.—p. 1163.  
Convulsive Therapy in Mental Disorders. N. M. Owensby, Atlanta, Ga.—p. 1164.  
Prophylactic Use of Pertussis Vaccine (Sauer): Report of Results in Private Practice. C. Howell, Baltimore.—p. 1166.  
Meningococcal Meningitis: Observations in 157 Cases in the Louisville City Hospital. T. C. Smith, Louisville, Ky.; W. T. Maxson, Lexington, Ky., and D. F. H. Murphy, Louisville, Ky.—p. 1168.  
Elliott Therapy of Pelvic Inflammations in the Negroes. G. A. Williams, Atlanta, Ga.—p. 1171.  
Syringe Adaptor for Rectal Use. M. H. Prosperi, Washington, D. C.—p. 1174.

**Lung Abscess Treated with Sulfanilamide.**—Murphy and Frere successfully treated a case of abscess of the lung caused by the hemolytic streptococcus with sulfanilamide. They believe that the use of the drug in their case caused immediate symptomatic and clinical improvement and perhaps

shortened the duration of the disease. When hemolytic streptococcus infection is found in the acute stage of pulmonary suppuration sulfanilamide is worthy of trial, provided no contraindications exist.

**Dinicotinic Acid in Pellagra in Relapse.**—Vilter and her associates used dimethyl dinicotinic acid (2,6-dimethylpyridine-3,5-dicarboxylic acid) or dinicotinic acid (3,5-pyridine dicarboxylic acid) in treating nine pellagrins in relapse and two nonpellagrous persons. These patients received orally from 500 to 1,000 mg. of the acid daily. Each acid, although soluble with difficulty, was completely dissolved in water before administration. The nine pellagrins were severely ill. Some temporary improvement was observed in five of the patients, the response being characterized by an increased feeling of well-being and a partial decrease in the fiery redness of the tongue. The subsequent administration of nicotinic acid, however, elicited a more complete response. The physiologic response to these drugs was quite different from the response to nicotinic acid. Neither oral nor intravenous administration has been found to produce the flushing reaction and rise in cutaneous temperature which occur after similar doses of nicotinic acid. Observations show that 2,6-dimethyl dinicotinic acid and dinicotinic acid have only a partial beneficial effect on pellagra in relapse and they should not be used as a substitute for nicotinic acid. The authors feel that protein deficiency in pellagra is of more importance in the syndrome of pellagra than is currently stressed and that perhaps a close interrelationship exists between protein metabolism and the role of nicotinic acid. At any rate a well balanced high caloric diet should be administered simultaneously with the nicotinic acid.

### Texas State Journal of Medicine, Fort Worth

34:391-454 (Oct.) 1938

- Earlier Recognition of Intra-Abdominal Malignant Lesions. W. Walters, Rochester, Minn.—p. 397.  
Patent Urachus. H. Dudgeon Jr., Waco.—p. 401.  
Treatment of Gas Gangrene Infections. J. J. Faust, Tyler.—p. 404.  
\*Comparative Study of Foille with Tannic Acid and Tannic Acid Preparations in Treatment of Burns. T. C. Terrell, Fort Worth.—p. 409.  
Recent Advances in Hematology. E. E. Osgood, Portland, Ore.—p. 416.  
Thrombocytopenic Purpura. D. Neighbors, Fort Worth.—p. 419.  
Anemia in the Aged (Syndrome of Kyphosis, Gastric Hernia and Anemia). H. M. Winans, Dallas.—p. 422.  
Study of Children Born of Positive Reactor Tuberculous Mothers. E. A. Wright, Houston.—p. 424.  
Diethylene Glycol Poisoning: Report of Case with Necropsy Findings. P. Brindley and M. P. Kelsey, Galveston.—p. 426.  
The Ultraviolet Ray as an Eye Hazard. V. D. Rathgeber, Fort Worth.—p. 431.  
Nasal Physiology and Its Relation to Sinus Surgery. J. M. Robison, Houston.—p. 434.

### Comparison of Preparations Used for Treating Burns.

—Terrell gives the composition of foille (0.14 per cent of potassium iodide, 0.25 of calcium iodide, 0.39 of calcium soap, 0.02 of calcium thiosulfate, 0.086 of calcium sulfite, 0.1 of oxyquinoline sulfate, 1.4 of ethyl alcohol by volume, 2.8 of phenol, 1.3 of ethyl aminobenzoate, 3.4 water, 90.11 of vegetable oil and sulfur and glycerin present) used in the prolonged treatment of burns. It is not toxic nor does it cause any detrimental systemic reactions. Its formula has been clinically tested with reference to analgesic, antiseptic and healing properties. Dogs have been used for experimental purposes. It has been used on human patients to a sufficient extent to warrant its recommendation in the treatment of all recent wounds and burns. It has been found safe to use in extensive as well as minor burns. The preparation has been tested on several occasions and found to have a low phenol coefficient, but in spite of this and its phenol content it has been proved that it is not injurious to the tissues when used in concentrated form. A thick layer of the medication is applied and a sterile dressing is placed over the wound. The wound is kept constantly bathed with the emulsion for forty-eight hours; then the dressing is removed and the preparation is reapplied. Thereafter, two or three applications are required each day until healing is complete. Experimentally, the burns of dogs treated with it healed much more rapidly and with considerably less discomfort than those treated with 10 per cent tannic acid or with either of two proprietary tannic acid preparations. The preparation offers a much shorter convalescence to the patient, with more comfort and less scarring, without the danger of toxic manifestations.

### FOREIGN

An asterisk (\*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

### British Journal of Children's Diseases, London

35:165-240 (July-Sept.) 1938

- Exophthalmic Goiter in Children. F. R. B. Atkinson.—p. 165.  
Treatment of Diphtheria and Scarlet Fever by Active Immunization. K. Sedláček.—p. 175.  
Congenital Cardiac Pentad: Fallot's So-Called Tetralogy Together with Common Interventricular Orifice. W. M. Feldman and Sheila G. Snook.—p. 183.  
Morbili Bullosi: Report of Fatal Case. E. James and A. A. Miller.—p. 191.

### British Journal of Experimental Pathology, London

19:273-366 (Oct.) 1938

- Antigenic Differences in Strains of Epidemic Influenza Virus: I. Cross Neutralization Tests in Mice. T. P. Magill and T. Francis Jr.—p. 273.  
Id.: II. Cross Immunization Tests in Mice. T. Francis Jr. and T. P. Magill.—p. 284.  
Serologic Races of Influenza Virus. W. Smith and C. H. Andrewes.—p. 293.  
Rate of Absorption of Carcinogens and Local Tissue Reaction as Factors Influencing Carcinogenesis. P. R. Peacock and S. Beck.—p. 315.  
Failure of Acute and Subacute Inflammation to Influence Carcinogenesis with 3:4-Benzpyrene. S. Beck.—p. 319.  
Susceptibility of Voles to Human and Bovine Strains of Tubercle Bacilli. A. Q. Wells.—p. 324.  
Specific Character of Stage of Aggregation in Agglutination and Precipitation of Antibody-Antigen Compounds. J. T. Duncan.—p. 328.  
\*Microscopic Observations on Bacteriophage of Bacterium Coli. K. B. Merling-Eisenberg.—p. 338.  
Functional Hyperplasia of Parathyroids in Experimental Anemias. A. B. Eisler.—p. 342.  
Role of Adrenal Gland and of Raised Metabolism in Production of Organ Hypertrophy in Thyroid-Fed Rat. O. L. V. S. de Wesselow and W. J. Griffiths.—p. 347.  
Study of Experimental Immunity to Virus of Psittacosis in the Mouse, with Special Reference to Persistence of Infection. S. P. Bedson.—p. 353.

**Bacteriophage of Bacterium Coli.**—The studies performed by Merling-Eisenberg demonstrate the particulate nature of the bacteriophage of Bacterium coli. They point in the same direction as experiments of Elford, Andrewes and Tang (1936) and of McIntosh and Selbie (1937), who have shown by centrifugation that the bacteriophage action is bound to an agent of particulate nature. Because of their small size the bacteriophage bodies are not visible in transmitted light or stained preparations, which were the methods used by Wollmann (1925). d'Herelle (1926) has not observed any motion of the bodies within the bacterial cells, and he also reports only between fifteen and twenty-five bodies released from one bacterium. This is no doubt due to the optical system which he has employed. It obviously enabled him to perceive only the coarser granulate disintegration of the membrane into from fifteen to twenty-five particles, but not the ten times greater number of the much fainter bacteriophage bodies. The bacteriophage is distinguished from non-specific particles and its size is found to be 25 millimicrons.

### British Medical Journal, London

2:875-928 (Oct. 29) 1938

- States of Depression: Their Clinical and Etiologic Differentiation. A. Lewis.—p. 875.  
\*Clinical Significance and Estimation of Blood Vitamin B<sub>1</sub>. E. N. Rowlands and J. F. Wilkinson.—p. 878.  
Treatment of Brucella Abortus Infection with Fuadin and Prontosil. A. P. Thomson.—p. 884.  
Report on Five Cases of Brucella Abortus Infection. M. Gaffney.—p. 885.  
\*Suppression of Lactation by Oral Estrogen Therapy. G. L. Foss and P. Phillips.—p. 887.

**Significance of Blood Vitamin B<sub>1</sub>.**—Rowlands and Wilkinson established that the phycomyces test, based on Schöpfer's discovery (1935) that the growth of the mold *Phycomyces blakesleeanus* was proportional within certain limits to the amount of vitamin B<sub>1</sub> present in the medium, is a fairly reliable method of estimating vitamin B<sub>1</sub>. They determined the standard range for normal blood, taken from healthy members of the departmental staff, who gave figures ranging between 6.5 and 16.5 micrograms per hundred cubic centimeters of blood. Estimations were also carried out on a series of patients suffering



from alcoholic neuritis, nonalcoholic polyneuritis, subacute combined degeneration, diabetic neuritis, nutritional neuritis, anemias, and cardiovascular, renal and endocrine diseases. The investigations seem to show that gross vitamin B<sub>1</sub> deficiency is rare in England. This is not unexpected, since the daily requirement for the normal person is about 500 international units (1 mg. of pure vitamin B<sub>1</sub>): vitamin B<sub>1</sub> has a very wide distribution in foodstuffs and it is therefore almost impossible for the intake to be inadequate with a reasonable diet. This is in contrast to the position with vitamin C, the distribution of which is restricted to certain types of food. Nevertheless, vitamin B<sub>1</sub> deficiency may arise from an inadequate supply, inadequate absorption, inadequate utilization or through its destruction in the alimentary tract. In many of these deficiencies an inadequate dietetic intake leads to anatomic or physiologic changes within the intestine and then to diminished absorption, which in turn leads to further disorder of the intestinal function. Moreover, some balance between the specific nutritional elements, such as iron and vitamin B<sub>1</sub>, may be necessary. The only conditions in which a gross deficiency of vitamin B<sub>1</sub> was found were alcoholic neuritis, nutritional neuritis, scurvy and malnutrition. In these cases definite improvement followed the administration of vitamin B<sub>1</sub> (and vitamin C in the scorbutic patient). A partial deficiency was observed in simple achlorhydric anemia. The cases of subacute combined degeneration of the spinal cord gave normal figures; therefore the poor therapeutic results following the administration of vitamin B<sub>1</sub> obtained by workers in this field are not surprising. Similarly, the vitamin has not proved of much value in polyneuritis other than the alcoholic, gestational and nutritional forms. This observation corresponds with the values for blood vitamin B<sub>1</sub> found in this series. It appears, therefore, that the changes in the nervous system in these conditions, though clinically similar to those reported in beriberi, have a different etiology and are not associated with vitamin B<sub>1</sub> deficiency. There is no clinical evidence that vitamin B<sub>1</sub> is concerned in hemopoiesis, and this is corroborated by the normal figures given by this test in the uncomplicated primary anemias.

#### Suppression of Lactation by Oral Estrogen Therapy.

—Foss and Phillips state that experience in a few cases of acromegaly and thyrotoxicosis when attempting to inhibit the function of the anterior pituitary in human beings (Foss, 1937), together with Zondek's statement (1936) regarding the quantity of estrogen necessary to retard growth and gonadotropic function in rats, makes it difficult to realize that oral theelin in doses of from 20,000 to 30,000 international units given over a period of from two to six days can inhibit a function of the anterior pituitary. Normally this is held in check only by massive amounts of estrogen and/or progesterone in the placenta. It is much more possible, in the authors' opinion, that theelin acts specifically on the mammary gland, in some way preventing the action of the lactogenic hormone of the anterior pituitary or even by direct antagonism. At present an explanation of this clinical observation cannot be ventured. It is unlikely that such small doses will in any way influence the chemical constitution of human milk.

#### Journal Obst. & Gynaec. of Brit. Empire, Manchester

45: 769-892 (Oct.) 1938

- Lipoid Rich Granulosa-Cell Tumor with Discussion on Theca-Cell Tumor. J. G. Thomson and F. Stabler.—p. 769.
- Treatment of Myoma. P. Werner.—p. 780.
- \*Value of Urea Clearance Test in Pregnancy. Doris B. Brown.—p. 786.
- Disgerminoma of the Ovary, Associated with Masculinity: Case. A. Gough.—p. 799.
- \*Human Fetal Electrocardiogram. G. H. Bell.—p. 802.
- Duplication of the Hind End of an Anencephalic Fetus. A. E. Harbeson.—p. 810.
- Effects of Intravenous Vasopressin on Toxemias of Pregnancy. E. de Valera and R. J. Kellar.—p. 815.
- Acute Inversion of the Uterus. J. H. Peel.—p. 821.
- Squamous Cell Carcinoma Occurring in an Ovarian Dermoid, with Secondary Involvement of Uterus, Fallopian Tube and Bowel: Case. R. B. Meiklejohn and J. A. Stallworthy.—p. 830.
- A Flying Fetus. R. W. Knowlton.—p. 834.

**Urea Clearance Test in Pregnancy.**—Brown presents the results of 671 urea clearance tests performed on 243 pregnant women. The urea clearance test was first determined for normal pregnant women and then tests were made both before and after

delivery on women with toxemia and on some patients who had pyelitis of pregnancy. A normal clearance test does not necessarily mean a normal kidney, as the test may be normal until from two thirds to three fourths of the renal tissue has been rendered functionless and also the clearance value is influenced by an alteration in the circulation rate and the supply of oxygen to the kidneys so that the results are lowered by severe anemia and cardiac decompensation. A low clearance value in an apparently well patient should be repeated and it must always be kept in mind that variations of less than 20 per cent are of no significance. The clearance results in the present series were less constant after than before delivery. Harrison says that in severe renal damage the clearance is more fixed than in normal persons. Each patient, therefore, must be considered separately. The urea clearance test extends but never replaces clinical investigation. The differential diagnosis between preeclamptic toxemia, chronic nephritis and essential hypertension is made much easier by the urea clearance test. Before delivery a high value excludes chronic nephritis and if the blood pressure remains high with little other evidence of toxemia and a high clearance the case is probably one of essential hypertension. If the clearance is low the result is of no value in pregnancy in the differentiation of preeclamptic toxemia, chronic nephritis and essential hypertension but the result after delivery is of great value—most patients suffering from preeclamptic toxemia show a rapid rise within a week or two of delivery, while in chronic nephritis the percentage rise is much less and the clearance never reaches a normal level. The follow-up of patients shows that if the clearance is high during the toxemia the prognosis is good even if the degree of toxemia is clinically severe, and the same may be said if the clearance rises to more than 100 per cent within a week or so of delivery even if the clinical condition lags behind. The clearance test is of most value several months after delivery when low tests show definite renal damage at a time when clinical signs may be slight or absent, although possibly on repeated clinical examination some evidence may be found in practically all cases. A low urea clearance is sufficient in the author's opinion to forbid a future pregnancy for at least two years, when further clinical examination and the clearance test should be repeated. Stander, Ashton and Cadden think that a urea clearance below 80 per cent is strongly suggestive of renal damage; therefore a further pregnancy is not wise. The clearance test is also useful during the treatment of toxemia; if the test is rising or remaining stationary, conservative treatment can be continued with confidence.

**The Human Fetal Electrocardiogram.**—Using a thermionic valve electrocardiograph susceptible of high amplification, Bell obtained electrocardiograms when leads were taken from the abdomen of pregnant women which show in some cases waves which are almost certainly fetal in origin. The evidence supporting the fetal origin is that the direction of the fetal deflection depends on the presentation (vertex or breech) and in a case of twin pregnancy two sets of deflections were obtained. Of thirty-three pregnant women examined in the last two months of pregnancy about one third showed positive results, but the other two thirds did not show any wave on the electrocardiogram which could be definitely recognized as fetal. It is suggested that the failure to secure positive results in all the electrocardiograms is due partly to differences in the electrical properties of the abdominal wall and partly to the electrical disturbances produced by the abdominal muscles, and not to insufficient sensitivity of the apparatus.

#### Lancet, London

2: 867-928 (Oct. 15) 1938

- Bacteremia. J. A. Ryle.—p. 867.
- Treatment of Ankle Fractures. W. G. Campbell.—p. 872.
- \*Oxygen Therapy, with Note on a New Nasal Mask. R. V. Christie.—p. 876.
- A New Chemical Contraceptive. J. R. Baker, R. M. Ranson and J. Tynen.—p. 882.
- Cardiac Convulsion Therapy in Nonschizophrenic Reaction States. L. C. Cook and W. Ogden.—p. 885.

**Oxygen Therapy.**—Christie states that there are broad principles which must be appreciated if oxygen is to be used with understanding. The first principle concerned is that blood flowing through a healthy lung is more or less completely saturated with oxygen. The second principle is that cyanosis or lack of

oxygen does not cause dyspnea. The relief of dyspnea is of no significance in determining the value of oxygen therapy. The third principle is that if oxygen is given at all it should be given continuously. To give oxygen once every two hours to a patient with bronchopneumonia may be equivalent to placing him on top of Mount Everest and bringing him back to sea level every two hours for a "brcather." Most authorities are agreed that the intermittent administration of oxygen is probably worse than useless. Anoxemia can embarrass the heart of a healthy person; therefore the life of a patient with bronchopneumonia or acute pulmonary edema may depend on the efficient administration of oxygen. The indiscriminate administration of oxygen to any patient who is cyanosed and acutely ill is in part responsible for the conflicting evidence on the value of oxygen therapy. Oxygen should be given only when it is reasonable to expect that it will relieve the anoxemia. When cyanosis is due to localized consolidation or to localized collapse of the lung, it can seldom be relieved by oxygen. When cyanosis is due to a generalized impairment of aeration or to an inflammatory process scattered throughout the lung, oxygen, if properly given, should relieve cyanosis. An adequate supply of oxygen is as important as the method used for its administration. The most satisfactory methods for the administration of oxygen are the nasal catheter, the nasal mask and the oxygen tent. The nasal catheter is often too uncomfortable for continuous use if oxygen is given in amounts adequate for an adult. In infants the catheter may be satisfactory. The nasal mask is efficient, comfortable and inexpensive. A nasal mask for oxygen administration is described that combines efficiency with simplicity of operation and assures the comfort of the patient.

### Medical Journal of Australia, Sydney

2: 585-626 (Oct. 8) 1938

- Symptomatology and Treatment of Bites of Australian Snakes. C. H. Kellaway.—p. 585.  
Pirates and Buccaneers. L. Duncan.—p. 589.  
Outbreak of Gastro-Enteritis: Suspected Food Poisoning with Milk as a Possible Vehicle. J. Dale.—p. 591.  
Consideration of General Anesthesia for Dental Surgery. N. E. Heath.—p. 594.  
A Postgraduate Holiday. J. B. Hamilton.—p. 599.

### South African Medical Journal, Cape Town

12: 613-654 (Sept. 10) 1938

- \*Rickettsioses of South Africa. A. Pijper and C. G. Crocker.—p. 613.  
A Mountain Stretcher. G. A. P. Ross.—p. 630.  
Onyalai: A Form of Purpura Occurring in Tropical Africa: Report of Cases Occurring in South Africa. J. Gear.—p. 632.  
Bantu Syphilis. S. V. Humphries.—p. 637.  
Amaas. G. G. Hay.—p. 639.  
The Position of General Hospitals in South African Health Organization. H. S. Gear.—p. 642.  
Note on Anopheles Gambiae Giles and Anopheles Coustani Variety Tenebrosus Donitz from Southern Africa. B. de Meillon.—p. 648.  
Heredity in Nervous and Mental Disease. S. Berman.—p. 651.

12: 655-690 (Sept. 24) 1938

- The Unholy Triad: Tuberculosis, Venereal Disease, Malnutrition. P. W. Laidler.—p. 658.  
Obstetrics: Ancient and Modern. J. A. Lloyd.—p. 666.  
Surgical Aspects of Endocrinology. A. G. Sweetapple.—p. 669.  
The Medical Aspect of Endocrine Disease. J. S. Alexander.—p. 673.  
The Gynecologic Aspect of Endocrine Disease. D. F. Standing.—p. 676.

12: 691-742 (Oct. 8) 1938

- Chemoprophylaxis of Malaria in Portuguese India. I. Froilano de Mello.—p. 710.  
Wild Animals as Carriers of Infection. G. de Kock.—p. 725.

**Rickettsioses of South Africa.**—Pijper and Crocker believe that the three South African rickettsioses (tick-bite fever, murine or rat-flea or sporadic typhus and louse typhus) have been insufficiently studied, especially as regards their relationship with rickettsioses of other countries. Cross immunity tests have been performed only between tick-bite fever and spotted fever, with quite negative results, and by means of immune serum it has been shown that tick-bite fever and Rocky Mountain spotted fever probably have little in common. The need for further work in this and other directions is stressed, because there is evidence that the three South African rickettsioses form a group by themselves, possessing closer affinities

with one another than with rickettsioses of other countries. The virus of tick-bite fever is not filtrable, does not produce lesions in rabbit's eyes and the authors were unable to cultivate it on the chorio-allantoic membrane. A brief experiment showed that heartwater and tick-bite fever have nothing in common, although the two can be conveyed by the same tick. The contention that South African epidemic typhus is not identical with classic typhus is based on the results of Weil-Felix tests on patients: lower titer of X 19, good agglutination of X 2 in many cases, sometimes agglutination of X K. The authors have now confirmed this serologic difference by studying the agglutinin titers of a large number of rabbits infected with their Basutoland strain of epidemic typhus. In sporadic typhus in South Africa a virus was found that proved to be immunologically identical with a virus in rats. It protected against tick-bite fever but not against epidemic typhus. Epidemic typhus gives protection against this virus, as it does against tick-bite fever. The authors have now studied the agglutinin curves of several cases of this sporadic typhus and confirm in detail previous observations: agglutination of both X 19 and X 2 and sometimes also of X K. This sporadic form of typhus dies out in guinea pigs when brain injections are used; the epidemic form can be kept going indefinitely by this method.

### Chinese Medical Journal, Peiping

54: 201-300 (Sept.) 1938

- Peking Diets. R. A. Guy and K. S. Yeh.—p. 201.  
Foreign Bodies in Urinary Passage. H. E. Shih.—p. 223.  
Studies on Control of Fecal-Borne Diseases in North China: VI. Epidemiology of Ascaris Lumbricoidea in an Urban Population. G. F. Winfield and T. H. Chin.—p. 233.  
Virulence and Immunogenic Activities of Vibrio Cholerae in Preparation of Cholera Vaccine. H. Yü.—p. 255.  
\*Use of Sodium Carbonate for Concentration of Tubercle Bacilli in Sputum. B. H. Y. T'ang.—p. 259.  
Fever Therapy by Electric Means and Its Rationale. H. C. Vassiliadis.—p. 271.  
Congenital Cataract. S. Y. Li.—p. 277.

#### Sodium Carbonate for Concentrating Tubercle Bacilli.

—T'ang examined 481 specimens of sputum from patients known to be suffering from pulmonary tuberculosis both by Petroff's 3 per cent sodium hydroxide method and by the sodium carbonate method. (Sodium carbonate in a solution of 7 per cent, allowed to act on the sputum for thirty minutes at a temperature of 65 C., is recommended to replace sodium hydroxide.) Other sputums (132) were examined by the direct smear method made from selected portions of the whole sample before being divided into two portions and further examined by the two concentration methods. It was found that sodium hydroxide concentration revealed only 4 per cent more positive sputums than direct smears, whereas the sodium carbonate method added 26 per cent. Bacilli are found more readily and in larger numbers after sodium carbonate concentration than in direct smears or after sodium hydroxide concentration. A more critical study of established methods of sputum examination was made on five sputums known to contain tubercle bacilli in small numbers. After the preparation of two direct smears from carefully selected particles of the crude sputum, it was divided into four equal portions. One portion of each sputum was treated by one of the four following methods: Pottenger's dilution-flotation, antiformin digestion, Petroff's sodium hydroxide concentration and the sodium carbonate concentration. Two smears of as nearly as possible the same size and thickness were made from each preparation and stained by the Ziehl-Neelsen method. It is probable that actually greater numbers of bacilli were seen after concentration by the sodium carbonate method than after dilution and flotation, as by the former method clumping of bacilli was commonly observed, whereas an even distribution of isolated bacilli was obtained by the latter method. The strongest recommendation for the use of sodium carbonate comes from a consideration that in the year 1936, when sodium carbonate was first used for concentration, the percentage of positive results increased by 7 per cent. During this year there was an increase in the total number of specimens examined. This was not due only to the fact that more patients were being seen but also to repeated examinations of carefully collected specimens of sputum from patients whose sputums were previously reported negative for tubercle bacilli.

**Presse Médicale, Paris**

46: 1521-1536 (Oct. 15) 1938

- Angina Pectoris Is a Unit. V. Audibert and Mlle. Legré.—p. 1521.  
 \*Epilepsy in Cerebral Tumors. J.-A. Chavany and A. Placa.—p. 1522.  
 Sterility Due Principally to Chronic Gonorrhea. C. Bécère and Elie François.—p. 1525.  
 Ouabain Arnaud. C. Dimitracoff.—p. 1527.

**Epilepsy in Cerebral Tumors.**—Chavany and Placa state that epilepsy may appear either in typical or in somewhat abnormal forms during any phase of the clinical evolution of cerebral tumors. On the basis of personal observations in hundreds of cases they encountered it in about 15 per cent of the cases, whereas other investigators give percentages of 21, 30 and even 41. After a brief review of the literature the authors point out that epilepsy can be observed as a secondary sign, connected with ventricular dilatation or cerebral edema, in all forms of cerebral tumors. It appears in three forms: (1) generalized attacks analogous to those of essential epilepsy, (2) abortive (petit) attacks with short loss of consciousness and without convulsive manifestations, and (3) Bravais-jacksonian attacks. Frequent Bravais-jacksonian attacks, which remain similar for months or years, suggest the existence of a cerebral tumor affecting the pyramidal tract in the neighborhood of its origin. Conversely, Bravais-jacksonian attacks that occur less close together (months apart) and perhaps change their aspect suggest, in the absence of the syndrome of intracranial hypertension, an encephalitis and, if an intracranial hypertension exists, they suggest encephalitis or a tumor of extrapyramidal localization. But although in the presence of Bravais-jacksonian attacks that are far apart and polymorphic and are not accompanied by intracranial hypertension the possibility of a cerebral tumor can be excluded, in the presence of numerous and identical Bravais-jacksonian attacks, it is impossible to make a distinction between encephalitis and tumor, since encephalitis may also cause such a clinical picture. The generalized epileptic attacks are often without value for the localization, except that they are often the first sign of a lesion of a mute zone. In case of the abortive (petit) epileptic attacks a temporal localization should be searched for. The Bravais-jacksonian attacks, which have considerable localizing value, constitute often the alarm signal of a compression of the cerebral origins of the pyramidal bundle. The author further calls attention to the considerable prognostic value of epilepsy and particularly of Bravais-jacksonian epilepsy. A long phase of Bravais-jacksonian attacks, more or less close together, and constituting the only symptom, indicates a malignant tumor. However, it is impossible to distinguish only by clinical means an extracortical meningioma from an intraparenchymatous fibrous glioma. On the other hand, Bravais-jacksonian attacks, which are less numerous and which precede, accompany or follow the appearance of a rapidly progressing hemiplegia of the flaccid type, indicate nearly always the existence of a malignant tumor.

46: 1553-1568 (Oct. 22) 1938

- Treatment of Anginal Syndromes by 883 F (Diethylaminomethyl-Benzodioxane). A. Clerc, J. Sterne and J.-P. Lenoir.—p. 1553.  
 \*Behavior of Denervated Adrenal Medulla. H. Hermann.—p. 1554.  
 \*Repeated Perforations of Gastroduodenal Ulcers (Description of Two Unreported Cases). J. Gosset, M. Jouanneau and J. Allamand.—p. 1556.

**Denervated Adrenal Medulla.**—For three years Hermann and his collaborators have made studies on the denervated adrenal medulla. In this report he summarizes the results which are of interest in connection with the surgical treatment of arterial hypertension or of diabetes. The investigations revealed that, after the total resection of the secretory nerves of the adrenal medulla in dogs, this gland retains an important part of its functional properties. Its microscopic structure remains normal; it does not lose the power to elaborate its specific product, which is always detected in it in considerable amounts but in smaller quantities than in the tested capsules. The epinephrine thus stored is perfectly mobilizable either by direct electrical excitation of the chromaffin tissues or by pharmacologic agents possessed of epinephrine-secreting powers. Finally the denervated gland secretes in the chloralosed animal, and under the conditions of suprarenogular anastomosis, minimal quantities

of the sympathomimetic hormone. All these observations establish the fact that the adrenals can escape from the control of the central nervous system without losing their capacity to produce and secrete epinephrine. It demonstrates its autonomic functioning and justifies the analogy between the epinephrinogenic gland and the sympathetic ganglion. The author thinks that these experimental observations deserve to be taken into consideration by those who are interested in the surgical treatment of hypertension or of diabetes by means of the denervation of the adrenals or by means of splanchnicectomy.

**Repeated Perforations of Gastroduodenal Ulcers.**

Gosset and his associates say that in view of the rarity of reports on repeated perforations they were at first under the impression that this is an exceptional accident. After describing the clinical histories of two patients with repeated perforations, whom they recently observed, the authors say that in the literature of recent years they have found sixty-four cases of repeated perforations of gastric or duodenal ulcers, disregarding of course the perforations of postoperative jejunal ulcers, which are comparatively frequent. They admit that they are unable to estimate, even approximately, the incidence of repeated perforation but point out that Pearce observed thirty-three repeated perforations among 4,183 cases of perforated ulcers (about one in 145 cases). Other authors observed two in 227 cases, one in 120, one in seventy-eight, two in ninety and four in eighty-two. These figures indicate that this complication is far from being exceptional. Discussing the pathogenesis of repeated perforations, the authors point out that it has been suggested that they are especially frequent after simple sutures. However, others have shown that this can be explained by the fact that simple suture is the method most frequently employed in the treatment of the first perforation and that on the whole the percentages correspond to those of the diverse technics employed. Regarding the seriousness of the repeated perforations the authors say that it is estimated diversely by different authors, some considering it as extremely grave and others as more benign than the first perforation. Pearce, for instance, reports a mortality as 9 per cent for the repeated perforations as compared to 27 per cent for the primary perforations. To explain the latter figures it has been suggested that the peritoneum developed a sort of local immunity after the first perforation. Discussing the treatment in cases of repeated perforations, the authors say that it does not differ from the usual treatment of perforated ulcers. The choice of the method is determined less by the repetitious character of the perforation than by the size, the location and the callosity of the orifice. The authors think that in selecting the method the surgeon should take into account especially the tenacious character of the ulceration, which is the cause of the repeated perforation. They think that in repeated perforation either gastrectomy should be done immediately or a simple method should be chosen which is least likely to interfere with a subsequent gastrectomy.

**Strasbourg Médical**

98: 303-318 (Aug. 5) 1938

- Results of Treatment of Puerperal Infection by Neocarsphenamine. J. Kreis.—p. 303.  
 \*Treatment of Hypogalactia by Ultraviolet Rays. M. Pelletier.—p. 314.

**Treatment of Hypogalactia by Ultraviolet Rays.**

Pelletier reports the histories of three women in whom irradiation of the breasts with ultraviolet rays proved effective against hypogalactia, after galactagogue medications had been tried without appreciable results. Following a description of the cases, the author says that this irradiation of the breasts with ultraviolet rays was first recommended in 1924. He applies gradually increasing doses every other day, the irradiations lasting from two to thirty minutes. The maximum number of irradiations is fifteen, followed by maintenance irradiations twice a week for about a month. During the irradiation, petrolatum is applied to the mamilla. The case histories indicate that the distance from the lamp to the breasts is from 60 to 70 cm. The author does not think that the results obtained with the ultraviolet irradiation are due merely to autosuggestion but assumes with some of the earlier investigators that the irradiation counteracts a disturbance in the calcium and phosphorus metabolism. Moreover, the local hyperemia probably facilitates the secretion.

**Monatsschrift für Psychiatrie und Neurologie, Basel**

100: 1-128 (Sept.) 1938. Partial Index

- Pathogenesis and Clinical Aspects of Subarachnoid Hemorrhages (Hemorrhagic Leptomeningitis). I. Scheinker.—p. 9.  
Amnesic Aphasia, Visual Aphasia and Disturbance in Optic Conception. H. Scheller.—p. 33.  
\*Polyneuritis After Oral Administration of Medicaments Containing Sulfanilamide. J. Rost.—p. 92.  
Disturbances in Optic Perception in Hypoglycemia. A. Weil.—p. 98.

**Polyneuritis Following Sulfanilamide.**—Rost directs attention to undesirable secondary effects that develop following the administration of a sulfanilamide preparation that is widely used in the treatment of gonorrhea (uliron). Although the therapeutic results obtained with this preparation have on the whole been gratifying, disorders such as headaches, intestinal disturbances, vomiting and morbilliform and urticarial exanthems have been observed in about 30 per cent of the treated cases. These disorders are usually observed on the tenth day of the treatment but they disappear, after the medication is discontinued, without causing further sequels. Recently, however, polyneuritic symptoms have been observed. After citing a case that was described by Hüllstrung and Krause, Rost describes two cases of his own. Both patients developed a polyneuritis, with special involvement of the motor component, after they had been subjected to sulfanilamide therapy, under the influence of which the gonorrhea had promptly subsided. The course of the polyneuritis was slow in both cases, but by the administration of vitamin B<sub>1</sub> the improvement could be somewhat accelerated. In the discussion of the pathogenesis of the polyneuritis it is pointed out that gonorrheal disorders as such have been known to cause neuritic symptoms in rare cases. However, in the first one of the cases discussed there was evidence that the polyneuritis was caused by the medication and not by the gonorrhea. Attempts have been made to solve the problem by animal experiments, but these have produced no satisfactory results as yet. It appears probable that the dosage of the preparation plays a part. In all cases in which neuritic disturbances were observed, the total dose was far in excess of that recommended by Schreus. For this reason it may be hoped that in the future such complications may be avoided by careful watching of the dosage.

**Schweizerische medizinische Wochenschrift, Basel**

68: 1181-1200 (Oct. 22) 1938. Partial Index

- Union and Division as Formative Processes in Embryologic Development. G. Wolf-Heidegger.—p. 1181.  
Incidence of Pulmonary Syphilis in Portugal. F. Wohlwill.—p. 1186.  
Bilirubin and Lipochromes in Blood. A. Gigon and M. Noverraz.—p. 1189.  
\*Acute Nicotine Poisoning During Extermination of Parasites by Means of Spray Method. H. Wehrli.—p. 1191.

**Acute Nicotine Poisoning from Parasiticide.**—Wehrli reports the clinical history of a man aged 24 who was hospitalized with tetaniform spasms in all four extremities, abdominal spasms, nausea, headache, excessive perspiration and tachycardia. The spasms disappeared after a short time. After describing the results of the general examination, the author says that the diagnosis proved difficult at first but that poisoning was thought of. The anamnesis revealed that the patient, who was a gardener, had sprayed a parasiticide consisting of a nicotine solution. The author cites similar cases from the literature which seem to indicate that the symptomatology of this type of nicotine poisoning varies considerably. Moreover, the symptoms resemble those of other intoxications and consequently do not permit a diagnosis. The latter is made possible by an exact anamnesis and by the chemical or biologic demonstration of nicotine in the excreta. The biologic test is based on the fact that, if a nicotine solution is dropped on the tongue of a frog, the animal responds by a peculiar curving contraction of the leg onto the back. In fatal cases, all organs contain nicotine. Since parasiticides that contain nicotine are used widely in agriculture and horticulture the author advises that, if acute intoxications are observed in gardeners and persons with similar occupations, nicotine poisoning should be promptly considered.

**Atti d. Soc. Ital. Ostetricia e Ginecologia, Rome**

34: 785-880 (Sept.-Oct.) 1938. Partial Index

- Technic and Value of Mastography After Introduction of Opaque Liquids in Galactophoric Ducts. A. Gusso.—p. 804.  
Gangrene of Feet from Ergotamine Injections in Early Puerperium. A. Gusso.—p. 826.  
\*Amount of Ascorbic Acid in Human Placenta. F. Rossi Marcelli.—p. 842.  
Interstitial and Submucous Fibromas of Uterus with Amenorrhea and Positive Friedmann Reaction. A. Duca.—p. 869.

**Ascorbic Acid in Human Placenta.**—Rossi Marcelli made quantitative determinations of the amount of ascorbic acid contained in ninety normal human placentas at different periods of evolution of pregnancy and at full term. He found that it varies within 1.32 and 1.58 mg. of ascorbic acid for each gram of placenta during the first six months of pregnancy and within 1.45 and 1.8 mg. of the acid for each gram of placenta during the last three months, after which it rapidly increases so that at full term it is twice as much as it was previously (within 3.96 and 4.85 mg. of ascorbic acid for each gram of placenta).

**Gazetta degli Ospedali e delle Cliniche, Milan**

59: 1011-1032 (Oct. 9) 1938

- \*Transfusion of Preserved Blood. I. Mingazzini.—p. 1011.  
Free Intra-Articular Bodies in Chondrosarcoma of Astragalotibial Joint. C. Leonardo.—p. 1017.

**Transfusion of Preserved Blood.**—Mingazzini gave preserved blood transfusions to twenty-six patients suffering from gastric or duodenal ulcers or from gastric cancer. The procedure was resorted to before or after a surgical intervention and in some cases transfusion was repeated. The blood had been stabilized by addition of sodium polyacetylenedioxysulfonate and preserved for from one to twelve days when it was administered to the patients. The results were similar to those which could have been obtained from transfusion with fresh pure blood. Unpleasant reactions, fever and changes in the urine did not take place. The crisis of the blood and the general condition of the patients improved in all cases. No doubt the administration of fresh pure blood is preferable whenever possible. But when not obtainable, as in many instances, blood stabilized with sodium polyacetylenedioxysulfonate and preserved for from one to twelve days can be used with safety. The technic for preparation of the blood and for transfusion is easy, the biologic and therapeutic properties of the blood do not diminish and the results are satisfactory.

**Giornale di Clinica Medica, Parma**

19: 1227-1334 (Oct. 10) 1938

- Experimental Investigations on Relation Between Glycemia and Chloremia. G. Battistini and P. Cavazzini.—p. 1227.  
Research for Presence of Iron in Human Testicles. I. Rizzi.—p. 1252.  
\*Metabolism of Creatine Bodies in Exudative Diatheses. C. Magi.—p. 1279.  
Evaluation of Allergy in Tuberculosis in Adults by von Gröer's Allergometric Method. Irene Miller.—p. 1295.

**Metabolism of Creatine Bodies in Exudative Diatheses.**—Magi found, in twenty-three infants and children who had an exudative diathesis, that the elimination of creatine and creatine bodies through the urine is diminished, in relation to normal, whereas that of creatinine is increased. According to the author, the diminished elimination of creatine and creatine bodies in the presence of an exudative diathesis is due to defective development of the muscles from alterations of the cellular metabolism of proteins and nitrogen substances with a consequent imperfect assimilation of the substances by the muscular tissues. The metabolic disorders originate in congenital endocrine and neurosympathetic disturbances.

**Minerva Medica, Turin**

2: 389-412 (Oct. 20) 1938. Partial Index

- Pyretotherapy and Index of Opsonins in Blood. G. Vernoni and A. Pirone-Naconetschnii.—p. 389.  
\*Lymphogranulomatosis Urethritis (Nicolas-Favre) in Women. A. Midana and Rita Leone.—p. 398.

**Lymphogranulomatous Urethritis in Women.**—Midana and Leone report eight cases of lymphogranulomatous urethritis in women. The patients had presented inguinal adenopathy in the past for periods of from one to five months. They com-

plained of a burning sensation at the urethra and had lymphogranuloma at the anus, rectum, vulva or external genitals and a positive Frei test. The urethral lesions could be seen either by simple examination or by urethroscopy. They were ulcerous, vegetative, associated ulcerous and vegetative, inflammatory or sclerotic and, in some cases, they were continuous with the external esthiomene. The disease was secondary to vulvar, anal, rectal or genital involvement in all cases. In certain cases, however, chronic lymphogranulomatous urethritis develops as the primary focus. When the disease is secondary to a primary lymphogranulomatous lesion, it originates in a propagation of the virus through the lymphatic channels with consequent disturbances of the local lymphatic circulation and damage of the tissues from direct contact with the virus.

### Anales de la Facultad de Medicina, Montevideo

23: 691-892 (Nos. 9-10) 1938. Partial Index

Infraperitoneal Drainage at Lumborenal Region. L. A. Surraco.—p. 691.  
Acute Form of Chagas' Disease: Case. R.-V. Talice, A. Alambarri and U. Regules.—p. 761.

Intestinal Perforation in Amebiasis. D. Mosto.—p. 836.

\*Rheumatism from Focal Infection. D. Quiroz.—p. 862.

**Rheumatism from Focal Infection.**—Quiroz made a clinical and roentgen study of fifty cases of rheumatism caused by focal infection from the teeth in thirty instances, the tonsils in seventeen and both the teeth and tonsils in three. Rheumatism from dental or tonsillar infection is either chronic, recurrent or polyarticular and it causes neither cardiac nor renal complications. Two of the fifty cases reported by the author were complicated by nonsuppurative, painful mastitis. He calls attention to the fact that mastitis has not been previously reported as a complication of focal infection. Treatment of the condition is surgical. It consists in early removal of the infectious focus followed by the proper medical, symptomatic, physiotherapeutic, antiallergic endocrine, dietetic and hygienic treatment.

### Archiv für Kinderheilkunde, Stuttgart

115: 65-128 (Oct. 14) 1938

Periosteal Bone Changes in Young Nurslings. O. von Chiari.—p. 66.  
Diphtherial Infection and Antitoxin Content of Blood. K. Fejes.—p. 86.

Scarlet Fever and Eosinophilia. G. Tamási.—p. 90.

\*Simultaneous Occurrence of Bronchial Asthma and Eczema and Their Reciprocal Modification During Childhood. F.-J. Casper.—p. 95.

Mastoiditis Complicated by Purpura Annularis Telangiectatica During Childhood. Margarete Wolf.—p. 114.

**Simultaneous Bronchial Asthma and Eczema.**—Casper says that all investigators agree that asthma and eczema are related and that they are symptoms of the same constitutional anomaly. The author investigated this relationship between asthma and eczema in 210 cases, giving especial attention to those in which asthma and eczema concur or alternate or in which eczema is to be found in the previous history. He describes in detail the histories of two children in both of whom there existed a hypersensitivity to milk, protein and in one case also to fats. Asthma developed for the first time when the eczema had disappeared and then the two disorders recurred alternately. In the second case there was evidence of a hereditary neuropathic component and the author suggests that neuropathy and exudative diathesis are related. He says that an allergic factor was noticeable in both cases but thinks that allergy does not explain the problem entirely. Studies on forty-two patients with chronic bronchitis and eczema revealed an asthmatic reaction in three. In all cases there were indications of a relation between eczema and bronchitis in that the bronchitic symptoms either alternated with the cutaneous manifestations or were accompanied by cutaneous exacerbations. The author further presents a report of seventy patients, thirty-nine of whom had both asthma and eczema and thirty-one only asthma. He shows that the essential factor in asthma as well as in eczema is the allergic constitution, which becomes manifest in a hypersensitivity of the organism to certain noxa, in vagotonic symptoms and in a tendency to eosinophilia. There exists a reciprocal action between eczema and asthma or bronchitis. If one of the two disorders is present in a severe

form the other one is mild or is completely absent. In this connection the author tells of a man in whom attacks of asthma and eczema alternated and who, by preventing the healing of the eczema, was able to suppress the attacks of asthma. The author thinks that, in view of the evidence of connections between asthma and eczema, the two should be considered as one and he applies the term *prurigo-asthma*. He also suggests that, since asthma with the attacks of suffocation is usually dreaded more than the eczema with its itching, it might perhaps be advisable in cases of alternate appearance of the two disorders to prevent the complete healing of the eczema.

### Beiträge zur klinischen Chirurgie, Berlin

168: 337-512 (Oct. 12) 1938. Partial Index

\*Relationship of Bone and Joint Tuberculosis to Pulmonary Tuberculosis. H. Frank.—p. 337.

Injury to Biliary and Pancreatic Ducts in Course of Resection of Duodenal Ulcer. M. Paraskevas.—p. 350.

Chloride Elimination in Bile in Hypochloremic Uremia Following Operations on Bile Passages. W. Nell.—p. 359.

Ointment-Plaster Cast Treatment of Wounds. H. G. Burgass.—p. 385.

Traumatic Consequences to Extremities. H. Angerer.—p. 391.

Question of Congenital Origin of Lateral Fistulas and Cysts of the Neck. J. Marx.—p. 435.

Transurethral Resection in Carcinoma of Prostate. H. Wille-Baumkauff.—p. 467.

**Tuberculosis of Bone and Joint and Pulmonary Tuberculosis.**—Frank investigated the relationship between bone and joint tuberculosis and pulmonary tuberculosis in 1,003 patients treated at the sanatorium of Heuberg. He finds that the simultaneous existence of pulmonary tuberculosis and bone and joint tuberculosis in infants and children is frequent. This is explained on the basis of the frequency and the regularity with which infection and reinfection take place at that age, as well as on the feeble resistance of young bodies. Simultaneous pulmonary involvement is equally frequent in somewhat older children; most of these exhibit advancing ulcerative pulmonary tuberculosis. Simultaneous involvement of the pulmonary tissue between the ages of 10 and 30 years is rare. The fact that most of the cases of bone and joint tuberculosis occur at this age suggests the possibility of the existence of isolated chronic tuberculosis of a single system. A spreading ulcerative pulmonary tuberculosis occurred in 2.4 per cent of all cases of joint-bone tuberculosis. The rest of the cases of pulmonary involvement presented benign forms of the disease, which is explainable by the existence of positive allergy of the body in bone and joint tuberculosis. The author does not consider the coexistence of pulmonary tuberculosis a contraindication to operative treatment of bone foci. Frequently the removal of a tuberculous focus exerts a beneficial effect on the entire organism.

### Münchener medizinische Wochenschrift, Munich

85: 1537-1576 (Oct. 7) 1938. Partial Index

Puerperal Sepsis. W. Schultz.—p. 1537.

Whooping Cough in Adults. H. Schlack.—p. 1541.

\*Benign Gastric Ulcers in Pernicious Anemia. W. Haring.—p. 1544.

\*Critical Remarks on, and Own Experiences with Cycloscope of Samuel R. Imbach.—p. 1545.

Experimental Gangrene by Heat Stasis and Anesthesia. H. Schwan.—p. 1546.

Duck Eggs as Cause of Two Epidemics of Enteritis in Military Kitchens. F. König.—p. 1550.

**Benign Gastric Ulcers in Pernicious Anemia.**—Haring points out that the close connections between the gastric mucosa and the hemopoiesis in the bone marrow lend considerable significance to the adenomas of the mucosa. In pernicious anemia there supposedly exists a disturbance in the so-called intrinsic factor which the healthy gastric mucosa probably forms by an incretory mechanism from the vitamin B<sub>12</sub> complex. Roentgenologic studies on the benign tumors which occur during pernicious anemia revealed to the author considerable secretory activity, and histologic studies on the tumors disclosed adenomas that were filled with colloid. He thinks that histologically they resemble the adenomas of the thyroid which occur in exophthalmic goiter or myxedema and suggests that the adenomas of the gastric mucosa might be related to the incretory activity. Surprising is the content in Hance-

mann's bodies, the nature and the significance of which are still unknown. The author realizes that further investigations on true polyps of the mucosa in pernicious anemia will be necessary to clarify the relation between the two disorders and he hopes that this report will stimulate such studies. He suggests that all patients with pernicious anemia and those with funicular myelitis traceable to pernicious anemia be subjected to roentgenologic examination of the stomach to detect possible polyps of the mucosa. Moreover, if polyps are detected by surgeons or roentgenologists the patient under observation should be subjected to internal examinations in order to detect possible relations to pernicious anemia or other hyperchromic anemias.

**Experiences with Cycloscope of Samuels.**—The original and new opinions expressed by Samuels on the menstrual cycle, ovulation, the periodic fertility and the early diagnosis of pregnancy (see abstracts in *THE JOURNAL*, February 26, page 696, and April 9, page 1241) induced Imbach of the women's clinic in Zurich to investigate Samuels' claims. Imbach made his studies with the cycloscope recommended by Samuels. In a considerable number of women between 21 and 45 years of age and in one man, the reduction time was determined daily over a period of seventy-five days. As recommended by Samuels, curves were plotted of the reduction time in order to obtain so-called cyclograms. It was found that the technic is not as simple as had been suggested by Samuels and that there are many sources of error; for instance, it was found that the reduction time differs after the hands have been bathed in warm or cold water. Moreover, there is a difference whether a thick or a thin fold of skin is clamped off. The results obtained by the author do not tally with those obtained by Samuels. In not a single one of the normal persons subjected to the cycloscope test did he obtain curves that approximated those of Samuels. He reaches the conclusion that Samuels' spectroscopic method does not reveal typical increases and decreases in the reduction time of the oxyhemoglobin within the monthly cycle and that the far-reaching and revolutionizing conclusions arrived at by Samuels lack a foundation that stands up under investigations.

### **Zeitschrift f. d. ges. experimentelle Medizin, Berlin**

104: 249-464 (Oct. 12) 1938. Partial Index

- Influence of Various Hormones on Prostate of Rat: Incretory Etiology of Hypertrophy of Human Prostate. F. Bühler.—p. 249.  
Mechanism of Takata Reaction: I. K. Dirr and M. Platief.—p. 292.  
Causes of Differences in Results of Determination of Serum Bilirubin According to Hijmans van den Bergh and Jendrassik and Cleghorn. K. Dirr and N. Sereslis.—p. 337.  
Temperatures and Vascular Conditions of Skin After Administration of Histamine to Human Subjects. O. Scheurer and R. Bauer.—p. 352.  
\*Effect of Intrapleural Injections of Hypertonic Solutions of Sugar During Exudative Pleurisy and Empyema. Bauer.—p. 364.  
Influence of Sex Hormones on Bleeding Time and Coagulation Time. F. Bühler and L. Bayer.—p. 376.  
Experimental Investigations on Antagonism Between Vogan and Thyroxine, with Observations on Action of Thyroxine on Heart. C. David.—p. 397.

**Hypertonic Sugar Solutions Intrapleurally in Pleurisy and Empyema.**—Bauer says that the conservative treatment of exudative pleurisy and the surgical treatment of empyema do not always produce satisfactory results and that a survey over the various methods of irrigation and instillation which have been recommended to accelerate cure and to avoid the formation of indurations and callosities reveals that none of the therapeutic methods satisfy completely. The results which Lexer obtained with the application of sugar to slowly healing wounds induced the author to resort to the intrapleural injection of hypertonic solutions of sugar in six cases of exudative pleurisy. It was thought that, by increasing the osmotic pressure in the exudate, a profuse fluid secretion could be obtained from the pleural endothelium. This was to prevent the formation of indurations or perhaps dissolve existing ones. It seemed possible also that the juxta-pleural parts of the lung could be favorably influenced by withdrawing water from them. It was assumed that, following this discharge of fluid, a better blood perfusion would result. However, no adequate action could be obtained in this manner, because the greatly impaired pleura likewise absorbs sugar rapidly, so that there is no pro-

longed osmotic action. To be sure, the author thinks that Spengler's method of treating spontaneous pneumothorax by means of hypertonic solution of dextrose is to be recommended, because the hypertonic sugar solution noticeably stimulates the resorptive action of the pleura. The observation that a mild osmotic stimulus accelerates the resorption of exudates suggests that, in the case of many of the substances that have been recommended for irrigation or instillation, not the particular composition but the stimulus on the pleura promoted the resorption.

### **Zeitschrift für klinische Medizin, Berlin**

135: 1-122 (Oct. 10) 1938. Partial Index

- \*Action Mechanism of Insulin. W. Brühl.—p. 1.  
Gastric Secretion and Sodium Chloride Tolerance. T. C. Afendulia.—p. 28.  
Clinical Characteristics of Bowl-Shaped Gastric Carcinoma. B. Fuchs.—p. 42.  
Physical Investigations on Circulation in Hypertension. H. Siedek and P. Riedl.—p. 88.  
Pathogenesis of Erythroblastic Anemia with Steatorrhea. F. S. P. van Buchem.—p. 95.

**Action Mechanism of Insulin.**—Brühl says that it is now generally conceded that insulin increases the motility and the secretory action of the stomach and that the last named action has led to the use of insulin in gastric diagnosis. In experiments on a large material, Kalk and Meyer gained the impression that in the action of insulin on the stomach the liver is in some manner involved. For this reason Brühl decided to investigate the action of insulin on the stomach of patients with hepatic diseases. He found that in severe disorders of the liver the latent period, that is, the time which elapses between the injection of insulin and the onset of the increased gastric secretion, is prolonged. He thinks that changes in the course of the blood sugar fluctuations are of causal significance in this delay: there is a flattening of the blood sugar curve, and the hypoglycemic values are reached later than is normally the case. Since the increase in gastric secretion that is observed after the administration of insulin is a result of the vagal irritation produced by the hypoglycemia, a retardation of the one must result in a retardation of the other. On the basis of blood sugar curves determined after administration of insulin in healthy persons and in patients with hepatic disease, the action mechanism of insulin is discussed and it is shown that the liver has an important part in the blood sugar fluctuations. It appears that the insulin blood sugar curve can be utilized for the detection of functional disturbances of the liver. However, the determination of the latent period of the gastric effect of insulin by means of the fractionated withdrawal of the gastric contents has sufficient reliability as a diagnostic aid only in the presence of severe hepatic impairment.

### **Zeitschrift f. menschliche Vererbungslehre, Berlin**

22: 129-260 (Sept. 20) 1938. Partial Index

- Historical Remarks on Term and Definition of "Diathesis." M. von Pfaundler.—p. 129.  
Familial Occurrence of Cleft Hand and Cleft Foot. Leonore Liebenam.—p. 136.  
Endemic Goiter and Malformation. L. von Unterrichter.—p. 160.  
\*Heredity of Allergic Diseases, Especially of Hay Fever. H. Sachsse.—p. 165.  
Investigations on Twins and Families Regarding Hereditary Pathology of Hyperthyroidism. W. Lehmann.—p. 182.  
What Conditions in Microscopic Structure of Chromosomes Are Responsible for Recessivity of a Gene. Gertraud Hasse-Bessell.—p. 258.

**Heredity of Allergic Diseases.**—In this discussion of the heredity of allergic diseases, Sachsse gives particular attention to hay fever. He reports studies on the families of thirty-eight patients with hay fever. The reports of some authorities on allergic diseases induced him to inquire in his hay fever patients and their families for disorders such as conjunctivitis during the spring months, asthma after contact with certain odors and substances, gastrointestinal disturbances after the ingestion of certain foods, and disorders such as urticaria, Quincke's edema, eczema, cholelithiasis, nephrolithiasis, gout, sciatica, rheumatism, migraine, exophthalmic goiter and gastric ulcer. On the basis of his studies he answers the question regarding the hereditary transmission of an allergic predisposition in the affirmative. However, environmental factors seem



to play an important part in the elicitation of an allergic symptom, so that it is possible that in one generation the allergic disposition is not so evident and that in an otherwise evidently dominant transmission it can be found that one generation has been missed. The author gained the impression that for a "strong" allergic predisposition it is necessary that at least two genes be present which carry an allergic tendency. Hay fever seems to become manifest only if at least two such genes concur, that is if either a "strong" predisposition is transmitted from one parent or a "weak" monomeric one from both parents. The author thinks that if two or more factors play a part it is understandable why the family anamnesis is not always so clear as is the case of monomeric dominant transmission. In this connection the author cites observers who assume a recessive transmission. In his own material the recessive transmission was contraindicated also by the fact that there were practically no marriages in relationship in the hay fever families investigated by him. He points out further that Hanhart's observation that in case of allergy in both parents not three fourths but only two thirds of the children are allergic might indicate a dimerous dominant transmission. He concludes that a complete and exact explanation of the mode of hereditary transmission requires further serial statistical studies, and especially investigations on twins.

### Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

82: 4649-4776 (Sept. 24) 1938. Partial Index

- \*Therapy of Encephalitis and of Related Neurotropic Infections of Nervous System. W. M. van der Scheer and R. Zijlstra.—p. 4666.
- Route of Inspiratory Air Current and Possibility of Aspiration from One Side of Nose into Lung of Same Side. H. A. E. van Dishoeck.—p. 4673.
- Measurement of Blood Pressure and Pulse Frequency in White Person in the Tropics and in Colder Climates. W. Radsma, J. T. Meijman and G. G. A. Mastenbroek.—p. 4679.
- Clinical Course of Fibrosarcoma, Spindle-Cell Sarcoma and Angiosarcoma of Soft Tissues. H. L. van Vierssen Trip.—p. 4692.

**Therapy of Encephalitis.**—Van der Scheer and Zijlstra direct attention to the use of methenamine in the treatment of encephalitis and of related neurotropic infections. After reviewing the literature on this treatment, they report the results obtained with it in more than 200 cases at the clinic for psychiatry and neurology in Groningen. A tabular report indicates that the material included patients with various forms of encephalitis, disseminated and transverse myelitis, postencephalitic parkinsonism, chorea minor, herpes zoster, radiculitis, Landry's paralysis, polyneuritis, poliomyelitis and others. On the basis of their experiences the authors recommend this treatment. They administer the methenamine in the form of a 40 per cent solution by means of intravenous injections. The individual dose is 10 cc., which usually is given every other day. The total dose is from 100 to 200 cc.

### Acta Radiologica, Stockholm

19: 207-312 (Sept. 30) 1938. Partial Index

- \*Roentgen Diagnosis of Tuberculous Spondylitis. N. Westermark and Gösta Forssman.—p. 207.
- Transparent Gas-Containing Cleft Formations in Gallstones and Their Significance in Roentgen Diagnosis. Å. Åkerlund.—p. 215.
- Sigmoid Volvulus of 360 Degrees Without Strangulation and With Insignificant Symptoms. B. S. Holmgren.—p. 230.
- Some Results of Irradiation with Soft Roentgen Rays at Small Focus Skin Distance (Contact Therapy). D. den Hoed.—p. 239.
- Unusual Ossification Center in Pelvis. Gösta Lindberg.—p. 350.
- Diagnosis of Extrapleural Abscess. H.-G. Skarby.—p. 259.

**Roentgen Diagnosis of Tuberculous Spondylitis.**—Westermark and Forssman demonstrate that from the roentgenologic point of view tuberculous spondylitis can be divided into a focal and a diffuse osteitis. The focal osteitis is more common in adults and the diffuse osteitis is more frequent in children. In focal spondylitis two different types are to be differentiated. One type is surrounded during the early stage by a circumscribed otosclerosis and by periosteal deposits; the other type is characterized by a rounded or irregular sequestrum and a rarefied border zone. Both types of focal spondylitis are localized most frequently in the anterior lateral border of the vertebral body. In focal spondylitis roentgenologic diagnosis is possible at an early stage, whereas in diffuse spondylitis the roentgenologic discovery is usually rather late.

### Hospitalstidende, Copenhagen

81: 917-944 (Sept. 20) 1938

- \*Treatment of Gangrene. H. Christensen and S. Hansen.—p. 918.
- Polycythemia Treated by Irradiation of Pyloric Glands and Brunner's Glands. F. Andersen, T. Geill and E. Samuelsen.—p. 933.
- Experiences with Meltzer-Lyon's Test. J. Agerholm-Christensen.—p. 940.

**Treatment of Gangrene.**—Christensen and Hansen report forty-eight cases of senile or diabetic gangrene of the extremities in thirty-three men and fifteen women with an average age of 69, given conservative treatment, supplemented by modern methods of wound treatment and modern treatment of diabetes. Attention was directed to keeping the dry necroses dry and to making the moist necroses dry in order that the necrotic tissue may mummify and be sloughed off; the result was often assisted by the amputation of one or two toes. The average hospitalization was ninety-five days. There was only one death from diabetic coma. Thirty-three patients (69 per cent) were discharged as recovered, twenty-four after conservative treatment, including slight operative intervention, nine after amputation of the leg.

### Norsk Magazin for Lægevidenskapen, Oslo

99: 1065-1176 (Oct.) 1938

- Acute Appendicitis in Small Children Aged Up to 5. P. Bull.—p. 1065.
- \*Cases of Progressive Muscular Dystrophy in Roving Norwegian Family. K. Wagner.—p. 1087.
- Case of Spontaneous Hyperventilation Tetany. K. Thomassen.—p. 1099.
- Widmark's Micromethod Applied in Determination of Ethyl Ether in Blood. O. Dybing.—p. 1105.

**Progressive Muscular Dystrophy in Family.**—Wagner examined fourteen of the affected members of the roving family in question, spread over the western part of Norway. There was paralysis without rigidity; of the patients with advanced atrophy accompanied by suspended or weakened tendon reflexes only three or four were so disabled that they had to be quiet. Of the thirty-five marriages that he traced in the family twelve, or about 35 per cent, were intermarriages, which he explains as due to social isolation. He concludes that a partially dominant factor is present, the affected persons being heterozygote with reference to the factor. The fact that three women, although undoubted bearers, have escaped the disorder may be accidental but may also mean that women are less liable to it than men. While the probability is not strong, he says, that nervous disorders are correlated with the muscular dystrophy, he found deafmutism in two cases in this family, epilepsy in one, manic-depressive insanity in one, mental unbalance in two, "queerness" in one and schizophrenia in one. There was also a criminal trend.

### Ugeskrift for Læger, Copenhagen

100: 1045-1068 (Sept. 15) 1938. Partial Index

- Serum Treatment of Type III Pneumonia. H. C. Gram.—p. 1045.
- \*Ascorbic Acid in Pregnancy, During Birth, in Puerperium and in Child's First Days of Life. A. Elmby and P. Becker-Christensen.—p. 1047.
- Foreign Bodies in Heart. F. Mehlsen.—p. 1051.
- "Scandinavian Disease" (Agranulocytosis After Amidopyrine Preparations). Johanne Christiansen.—p. 1054.

**Ascorbic Acid in Pregnancy, Puerperium and New-born.**—Elmby and Becker-Christensen made 4,000 determinations of the ascorbic acid in the blood, urine and milk in 200 women through the last five months of pregnancy and during birth and the puerperium, and determined the ascorbic acid in the umbilical blood and blood from the ear of the newborn. There was agreement between the ingested ascorbic acid and the spontaneous ascorbic acid concentration in the blood and milk. The titer of the serum ascorbic acid fell during pregnancy, whether the diet was deficient or rich in vitamin C, but not to excessively low values in the women whose diet was rich in vitamin C. The titer of the ascorbic acid in the serum in the newborn child depends on the concentration of the serum ascorbic acid in the mother and falls during the first ten days of life. The ascorbic acid concentration in the milk depends on the titer of the ascorbic acid in the mother's serum. By the additional administration of 100 mg. of ascorbic acid daily in the first ten days of the puerperium the ascorbic acid in the mother's serum and milk can be raised from subnormal to normal value. The titer of ascorbic acid in the child's serum follows that of the milk and therefore depends on the mother's diet.

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## THE ROLE OF POTASSIUM IN FAMILIAL PERIODIC PARALYSIS

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MONTREAL

This rare but fascinating disease was first described by Cavaré<sup>1</sup> in 1853 and later in 1874 by Hartwig,<sup>2</sup> who named it intermittent spinal paralysis. It is characterized by recurrent attacks of flaccid paralysis affecting mainly the muscles of the trunk and limbs, during which the deep reflexes disappear and the muscles become inexcitable to electrical stimulation. Attacks usually come on during sleep without previous warning; they last from a few hours to three or four days. In the interval muscular power is normal and the patient is entirely well. Attacks first make their appearance during childhood or adolescence and become less frequent or disappear in later life. Males are twice as often affected as females. Sporadic cases have been reported, but the condition is usually hereditary; Holtzapple<sup>3</sup> has described seventeen cases in four generations of the same sibship. Many theories have been advanced to explain these weird and crippling seizures.

The most comprehensive study of the disease has been made by Shinosaki,<sup>4</sup> who published his observations in twenty-four cases. Among the more important observations were the frequent (62 per cent) association of the disease with thyroid struma and the tendency for attacks to occur after administration of thyroid, epinephrine or diets high in carbohydrate. Hyperglycemia was often observed during the early stages of spontaneous attacks, and albuminuria was present during attacks in 73 per cent of the cases. Shinosaki carried out many ingenious experiments and concluded that the disease was a polyglandular syndrome in which the thyroid played an important part.

Our interest in the condition, and especially in the role of potassium, was aroused by the work of Herrington.<sup>5</sup> He reported the cases of two brothers who

averted paralysis by the ingestion of potassium citrate when prodromal symptoms appeared but he offered no explanation of the mechanism and carried out no metabolic studies. In 1901 Singer and Goodbody<sup>6</sup> administered potassium acetate to a patient with this disease in an attempt to promote diuresis and noted that attacks of paralysis became less frequent and severe. Holtzapple<sup>3</sup> had similar success with potassium bromide but attributed it to a sedative action of the bromide. Moreover, Biemond and Daniels<sup>7</sup> found a serum potassium value of 13.38 mg. per hundred cubic centimeters in a mild spontaneous attack and a value of 17.87 mg. during an interval but did not appreciate the significance of their results.

Since the commencement of our work, Aitken, Allott, Castleden and Walker<sup>8</sup> have reported their careful study of a patient with this disease. More recently Ferrebee, Atchley and Loeb,<sup>9</sup> Allott and McArdle<sup>10</sup> and Gammon<sup>11</sup> have published their observations. In agreement with their results we have found that attacks are associated with a marked fall of serum potassium and that administration of adequate amounts of potassium salts brings about rapid recovery.

We have produced attacks by administration of dextrose, epinephrine and ephedrine and have brought about recovery by injection of choline chloride carbamate (doryl) and acetyl- $\beta$ -methylcholine chloride (mecholy). Studies of electrolyte balance and the results of intravenous and intra-arterial injections of potassium chloride have thrown light on the mechanism of the attacks. A defect of creatine metabolism has also been observed, as noted in our preliminary report.<sup>12</sup>

L. H., a youth aged 18, has had recurrent attacks of paralysis involving the muscles of the trunk and extremities, and to a lesser extent the muscles of mastication and expression, since the age of 11. Similar attacks have occurred in the father, one brother and one sister.

The attacks almost invariably begin during sleep and last from twenty-four to forty-eight hours. He knows of no precipitating factors. Between the attacks he is active and feels perfectly well. Examination during the interval elicits no abnormality. Of late, attacks have been occurring several times each month.

The weakness begins in the muscle groups of the back and hips and within one or two hours extends to involve the neck,

From the Montreal Neurological Institute and the University Clinic, Royal Victoria Hospital and McGill University.

1. Cavaré: Observation d'une paralysie générale du sentiment et du mouvement affectant le type intermittent, *Gaz. méd. de Toulouse* 38, 1853.

2. Hartwig; Hermann: Ueber einen Fall von intermittierender Paralysis spinalis, *Inaug. Diss.*, Halle, 1874.

3. Holtzapple, G. E.: Periodic Paralysis, *J. A. M. A.* 45: 1224 (Oct. 21) 1905.

4. Shinosaki, T.: Klinische Studien über die periodische Extremitätenlähmung, *Ztschr. f. d. ges. Neurol. u. Psychiat.* 100: 564, 1926.

5. Herrington, M. S.: Successful Treatment of Two Cases of Familial Periodic Paralysis with Potassium Citrate, *J. A. M. A.* 108: 1339 (April 17) 1937.

6. Singer, H. D., and Goodbody, F. W.: A Case of Family Periodic Paralysis with a Critical Digest of the Literature, *Brain* 24: 257, 1901.

7. Biemond, A., and Daniels, A. P.: Familial Periodic Paralysis and Its Transition into Spinal Muscular Atrophy, *Brain* 57: 91 (June) 1934.

8. Aitken, R. S.; Allott, E. N.; Castleden, L. I. M., and Walker, Mary: Observations on a Case of Familial Periodic Paralysis, *Clin. Sc.* 3: 47 (July) 1937.

9. Ferrebee, J. W.; Atchley, D. W., and Loeb, R. F.: A Study of the Electrolyte Physiology in a Case of Familial Periodic Paralysis, *J. Clin. Investigation* 17: 504 (July) 1938.

10. Allott, E. N., and McArdle, B.: Further Observations on Familial Periodic Paralysis, *Clin. Sc.* 3: 229 (April) 1938.

11. Gammon, G. D.: Relation of Potassium to Family Periodic Paralysis, *Proc. Soc. Exper. Biol. & Med.* 38: 922 (June) 1938.

12. Pudenz, R. H.; McIntosh, J. F., and McEachern, Donald: The Role of Potassium in the Mechanism of Family Periodic Paralysis, *J. Clin. Investigation* 17: 530 (July) 1938.

the shoulder girdle and the upper and lower extremities. Weakness is occasionally hemiplegic in distribution at the onset but soon spreads to involve the opposite side. During severe attacks the patient is helpless and unable to make the slightest movement of the trunk or extremities. There is no disturbance of sensation.

Throughout the attacks he is depressed, irritable and uncommunicative and complains of headache, anorexia and nausea.

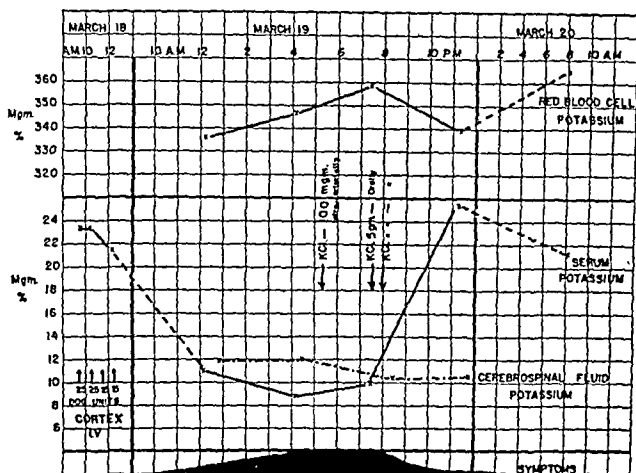


Chart 1.—Attack following adrenal cortex extract. The cerebrospinal fluid potassium did not alter with changes of serum potassium.

The pupils dilate widely and he is hypersensitive to light. The heart rate often drops to 40 beats a minute, and a systolic murmur develops at the apex. The skin is cool and the extremities are apt to be more moist than usual. The limbs are flaccid and the deep reflexes disappear while the superficial reflexes remain. During complete paralysis there is no muscular response to faradic or galvanic stimulation of nerve or muscle. Recovery of electrical reactions parallels the return to voluntary muscular power.

#### METHOD OF STUDY<sup>13</sup>

The patient was kept under observation for six months. Studies were made of eighteen separate attacks, of which eight were spontaneous and ten were induced. His intake of food and fluids and the collection of urine and stools were rigidly supervised. He received two standard diets which were alternated every three days. Expressed in grams, the two diets consisted of (a) protein 95, fat 68, carbohydrate 329 and potassium 3.73 and (b) protein 97, fat 110, carbohydrate 321 and potassium 3.93.

The potassium was checked by analysis of a duplicate diet. The sodium content was arrived at by calculation and the weighing of additional sodium chloride consumed. There was some variation of fluid intake as the result principally of the anorexia induced by the attacks, but at no time during the course of the experiment did the patient fail to consume the outlined diet. The urine was analyzed for potassium, sodium and chloride and the feces were analyzed for potassium. The urine was collected in twenty-four hour periods,

save during the attacks when determinations were made in six or twelve hour periods. Stools were analyzed in periods representing three days of excretion. Standard methods were used for the chemical determinations. Potassium was estimated by the method of Kramer and Tisdall.<sup>14</sup>

#### METABOLIC STUDIES

**Potassium.**—Blood Serum and Corpuscles: There was invariably a marked fall of serum potassium during the paralytic phase both in induced and in spontaneous attacks (charts 1 and 2). These values ranged from 7.7 to 12.4 mg. per hundred cubic centimeters during complete paralysis. In one induced attack a value as high as 17.4 mg. was found during almost complete paralysis. The critical level in our patient was therefore variable. With improvement of muscular power the serum potassium rose again toward normal. There was also considerable variation of serum potassium during the interval phase. It ranged from 17.5 to 30 mg. per hundred cubic centimeters, although it usually lay between 22 and 25 mg. In the case studied by Aitkin and his associates,<sup>8</sup> onset of paralysis occurred when the serum potassium fell to 12 mg. per hundred cubic centimeters. A patient studied by Allott and McArdle<sup>10</sup> showed weakness whenever the level fell below 16 mg. per hundred cubic centimeters. Determinations of corpuscular potassium were made during two attacks. The serum was separated immediately after the blood samples were drawn. We are not able to interpret the variations of potassium in the blood cells (charts 1 and 2).

**Intake and Output:** Despite a constant intake of potassium, the excretion varied quite markedly from

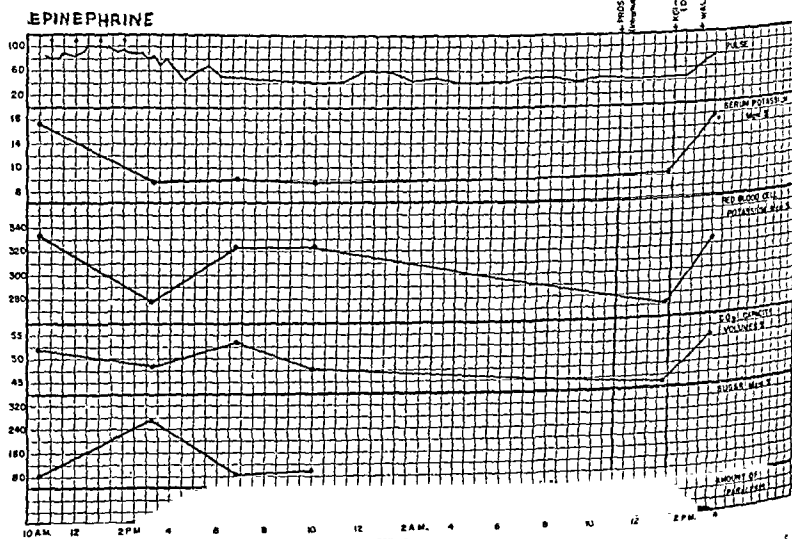


Chart 2.—Attack induced by epinephrine. No improvement after injection of 1.0 mg. of prostigmine intramuscularly. Note bradycardia and lowering of plasma carbon dioxide capacity during attack. Recovery after potassium chloride (5 Gm.) orally.

day to day. However, at no time was there any evidence of a positive or negative potassium balance over a representative period. During attacks there was a marked decrease in the excretion of potassium in the urine (chart 3), especially in the six hour specimens representing the phases of most marked paralysis. This was independent of urinary volume. A compensatory

13. Miss Constance Lambertus supervised the nursing and Mrs. Ruth Salter and Miss Doris Brophy made the chemical determinations.

14. Kramer, B., and Tisdall, F. F.: Clinical Method for Quantitative Determination of Potassium in Small Amounts of Serum, *J. Biol. Chem.* 46: 339 (April) 1921.

increase of output followed attacks. The first two attacks pictured in chart 3 were terminated by administration of potassium. The potassium content of the feces was variable but the total amount excreted was insignificant when compared to the urinary amount.

Cerebrospinal Fluid: During one attack the potassium content of the cerebrospinal fluid was determined

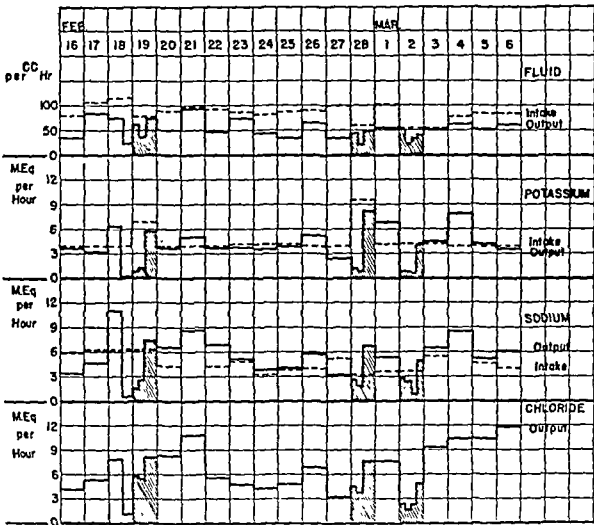


Chart 3.—Daily intake and urinary output of fluid, potassium, sodium and chlorides. The output of potassium, and to a lesser extent of sodium, is decreased on the days of the attacks. The latter are represented by the shaded areas. No diuresis of potassium preceded attacks.

on four different samples, representing stages from paralysis to almost complete recovery (chart 1). The values obtained varied from 10.3 to 12 mg. per hundred cubic centimeters, all of which were within the normal range of from 10 to 14 mg. There was no decrease corresponding to the lowering of serum potassium. The determinations covered a period of twelve hours, which seemed ample time for a change to become evident if

Range of Level of Inorganic Phosphate, Calcium and Sodium in Blood Serum		
	During Intervals, Mg. per 100 Cc.	During Attacks, Mg. per 100 Cc.
Serum inorganic phosphate.....	3.62- 4.75	2.74- 4.75
Serum calcium.....	10.4 - 11.8	10.1 - 11.4
Serum sodium.....	326.0 - 386.0	335.0 - 355.0

it was going to occur. A specimen of cerebrospinal fluid obtained during the interval phase contained 11.6 mg. of potassium per hundred cubic centimeters.

Other Electrolytes.—The urinary excretion of both sodium and chloride (chart 3) showed a slight decrease during the paralytic phase, followed by a compensatory increase during and after recovery. In the blood, the level of other important electrolytes was normal or without constant change during attacks. The range of numerous determinations is shown in the accompanying table.

Plasma Carbon Dioxide Capacity.—The carbon dioxide combining power of plasma was reduced moderately but consistently during attacks. Values obtained during two uninduced attacks were 50.4 and 52.9 volumes per cent. In one attack, induced by epinephrine, six values were obtained which varied from 43.5 to 53.7

volumes per cent. All values obtained during the interval phase have been above 64.4 volumes per cent.

Creatine and Creatinine.—Studies of creatine and creatinine in the blood and urine both during the attacks and in the interval phase have shown two definite abnormalities: (a) excretion of creatine in amounts up to 0.65 Gm. in twenty-four hours and (b) a highly variable daily excretion of creatinine, the range being from 0.78 to 2.13 Gm. in twenty-four hours. These abnormalities bore no constant relationship to attacks (chart 4). The blood creatine and creatinine have always been within normal limits (chart 5).

Sugar.—Numerous determinations of plasma dextrose have fallen within a normal range or within the range of expectation following administration of dextrose, insulin and epinephrine. When attacks have been induced by those substances the fall of serum potassium has not been related to hyperglycemia or hypoglycemia (charts 2 and 6).

Choline Esterase.—Determinations of acetylcholine esterase in defibrinated blood and in serum were made by the method of Ammon.<sup>15</sup> The activity of this enzyme was not abnormal either during or between attacks. The mean values for five determinations on serum made during attacks and five made during intervals were 50.4 cubic millimeters of carbon dioxide and 48.4 cubic millimeters of carbon dioxide respectively. These results are well within the range found for a large number of normal persons.

PRODUCTION OF ATTACKS

Spontaneous attacks were infrequent and attempts were made to induce them. We enjoyed fair but not invariable success with epinephrine, ephedrine, large doses of dextrose or dextrose combined with either insulin or epinephrine. The success of these measures must depend on the natural cycle of the disease at the

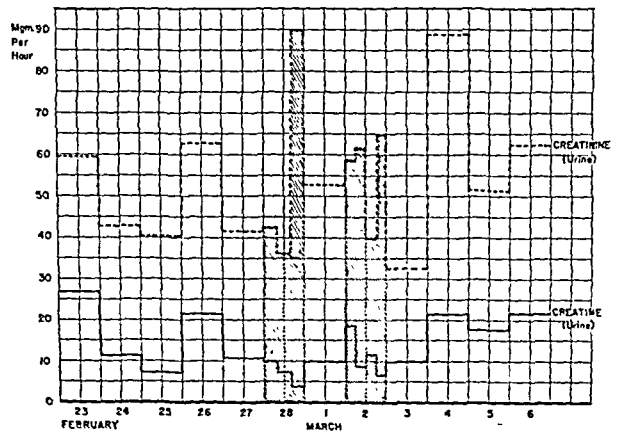


Chart 4.—Persistent creatinuria and marked daily variation in urinary creatinine. Shaded areas represent days of attacks.

time they are applied. In addition, frequent attempts to induce attacks seemed to lead to a refractory state; thus, four times in one week the administration of 200 Gm. of dextrose failed to produce an attack. Repeated use of the other substances led to similar failures.

Dextrose was given orally in amounts of from 200 to 250 Gm. at from 10 to 11 p. m. or in the early morn-

15. Ammon, R.: Die fermentative Spaltung des Acetylcholins, Arch. f. d. ges. Physiol. 233: 486, 1933.

ing. If paralysis occurred it developed within three or four hours. Sometimes paralysis was incomplete. Twice, when no paralysis developed, administration of 1 cc. of epinephrine at hourly intervals led to paralysis within two hours of the first injection. On one occasion the combined use of insulin and dextrose led to a typical attack.

Epinephrine was given subcutaneously in 1 cc. (1 mg.) doses at hourly intervals. The sum total on any one occasion was 5 cc. If paralysis was forthcoming it tended to appear within two or three hours of the first injection. Ephedrine sulfate  $1\frac{1}{2}$  grains (0.1 Gm.) was given each hour by mouth. The results were similar to those obtained with epinephrine. On one occasion paralysis developed within one hour of the first dose.

Adrenal cortex extract was tried on two occasions because of its ability to decrease sodium and increase potassium excretion. The first time 50 dog units of Connaught Laboratory extract was given. The second time 80 units was given intravenously, as described by Thorn and his associates.<sup>16</sup> Each time paralysis developed on the day following the test. These experiments were inconclusive in that (a) chemical studies failed to demonstrate any increase in urinary potassium following administration of adrenal cortex extract, (b) dextrose was also given prior to one of the attacks.

The lowering of the alkali reserve during attacks led to an attempt to induce paralysis by acidosis. Seven hundred grains (45 Gm.) of ammonium chloride was administered orally over a period of four days. The carbon dioxide combining power fell from its initial level of 69 volumes per cent to 35.9 volumes per cent but the serum potassium remained quite stable, at no

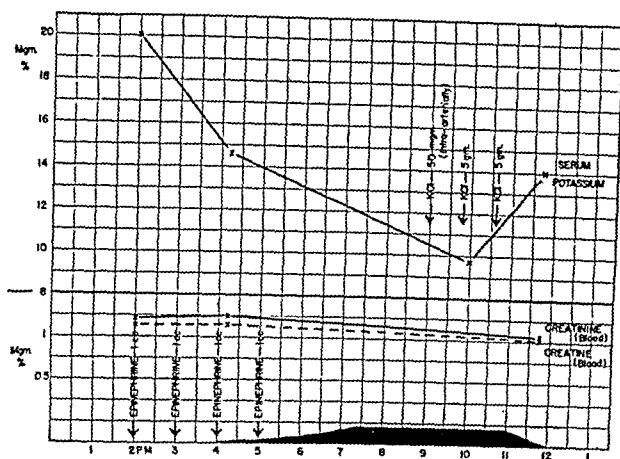


Chart 5.—Attack following epinephrine. Plasma creatine and creatinine remained stable. Injection of potassium chloride into brachial artery did not cause recovery in injected limb.

time falling below 17.9 mg. per hundred cubic centimeters. Slight weakness appeared in the back and the legs on the fourth day but no paralysis ensued.

No success followed an attempt to "wash out" potassium by large amounts of physiologic solution of sodium chloride intravenously, nor did lowering of the body temperature from 99.2 to 96.4 F. in a cold bath or taking severe and prolonged exercise lead to attacks.

16. Thorn, G. W.; Garbutt, H. R.; Hitchcock, F. A., and Hartman, F. A.: Effect of Cortin on Renal Excretion of Sodium, Potassium, Chloride, Inorganic Phosphorus and Total Nitrogen in Normal Subjects and in Patients with Addison's Disease, *Endocrinology* 21: 213 (March) 1937.

#### ALLEVIATION OF PARALYSIS

**Potassium.**—Administration of potassium has invariably resulted in prompt disappearance of the paralysis. We have used potassium chloride most often, but the citrate is equally effective, although somewhat larger doses are necessary to provide an equivalent amount of potassium.

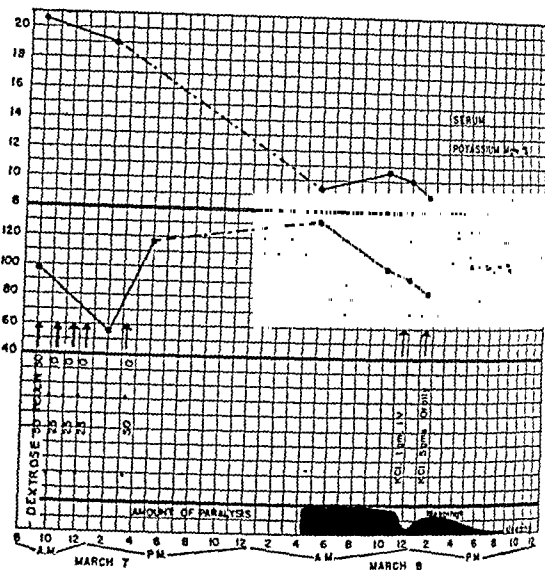


Chart 6.—Attack after dextrose and insulin. Lowering of serum potassium was not associated with hypoglycemia. Potassium chloride 1 Gm. intravenously caused partial recovery without elevation of serum potassium.

Potassium chloride, from 5 to 10 Gm. in watery solution by mouth, brought about return of movement within thirty minutes to one hour and the ability to walk unaided within two hours. Recovery was associated with a progressive rise of serum potassium (charts 1 and 2). Intravenous injection of potassium chloride caused much more rapid and dramatic recovery, the only disadvantage being intense burning pain along the course of the vessel even when the salt was injected in a concentration as low as 0.5 per cent. We usually injected 50 cc. of 2 per cent solution (1 Gm. of potassium chloride) during the course of ten minutes or less and did not exceed this amount. Severe thirst and cardiac extrasystoles sometimes occurred, but they disappeared when the injection was complete. Movement began to return in the limbs from four to eight minutes after the injection was begun, and the patient was able to stand within thirty minutes.

In his most severe attack the patient was almost unconscious and artificial respiration was necessary. Even the last rites of the church had been administered. Twenty minutes after the intravenous injection of 1 Gm. of potassium chloride the patient was sitting up and chatting. This amount was insufficient for complete recovery, however, and a further dose of the salt was given by mouth.

Since his discharge from the hospital four months ago, the patient has returned to full activity and has remained free from attacks. This has been achieved by the ingestion of 5 Gm. of potassium chloride each night as a prophylactic measure. Attacks had been occurring almost weekly prior to admission.

**Choline Esters.**—Acetyl- $\beta$ -methylcholine chloride (mecholyl) 25 mg., was injected intra-arterially on two occasions. Movement became perceptible in the limbs within eight minutes and progressed to complete recovery. Choline chloride carbamate (doryl) 0.25 mg. was injected during two attacks, once intravenously and

once intra-arterially. Generalized movement commenced in four minutes on each occasion and progressed to complete recovery. Complete recovery thus occurred within two or three hours in all four instances without administration of potassium, while the serum potassium rose to the normal level as muscular power improved (chart 7).

In all experiments atropine, from  $\frac{1}{15}$  to  $\frac{1}{50}$  grain (0.0009 to 0.0013 Gm.), was given prior to the choline esters to reduce unpleasant side effects. Atropine itself had no effect on the attacks save for the fact that it caused the heart rate to increase from about 40 to 120 a minute, showing that the bradycardia was of vagal origin.

**Other Drugs.**—Prostigmine methylsulfate was administered intramuscularly during four attacks..

On one occasion after 0.5 mg. there was steady improvement for an hour and a half and the patient could walk. The effect wore off after three hours and paralysis returned. A temporary but less marked improvement occurred another time following 1 mg. On the third occasion 1.5 mg. of prostigmine was without effect. In one attack the drug was given after potassium had been administered and recovery was much more rapid than with potassium alone. The drug seemed capable of potentiating the recovery mechanism but obviously did not supply the mechanism itself.

Ergotamine tartrate had no effect on the paralysis.

#### MECHANISM OF ATTACKS AND SITE OF ACTION OF POTASSIUM

The foregoing results show that paralysis is associated with a redistribution of potassium between the blood and the body tissues. It was at first suspected

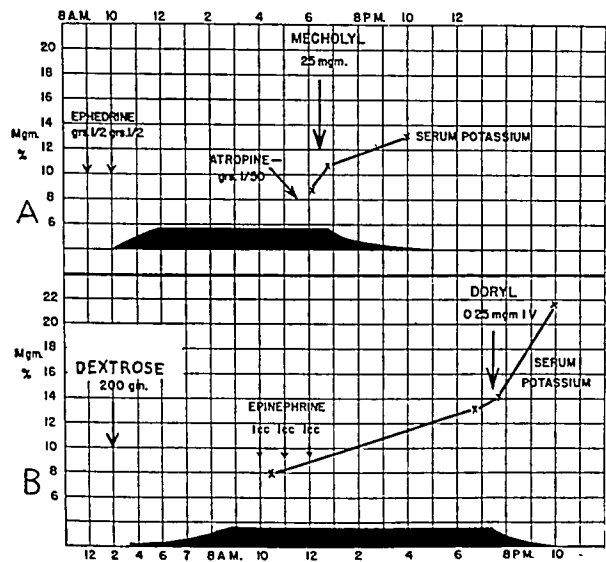


Chart 7.—A, attack induced by ephedrine and terminated by intra-arterial injection of mecholyl. B, attack induced by dextrose and ephedrine. Recovery followed 0.25 mg. of doryl intravenously. (Note the rise in serum potassium during recovery following injection of these choline esters.)

that the attacks developed because of abnormal loss of potassium from the body—a kind of potassium debt. This was disproved by balance studies. No undue loss of potassium preceded the attacks, and during the attacks excretion of potassium was greatly diminished. Indeed spontaneous recovery had often occurred without dietary or other sources of potassium, and this argued against depletion of the body's potassium stores.

During attacks the serum yielded its potassium to supply the demands of the tissues. On several occasions 1 Gm. of potassium chloride was given intravenously, improvement was rapid and the patient was walking within thirty minutes. During such partial recovery the serum potassium remained low, however, indicating that the injected potassium was leaving the serum and going elsewhere (charts 6 and 8).

Where then did the lack of potassium operate to produce paralysis and where did injected potassium remedy

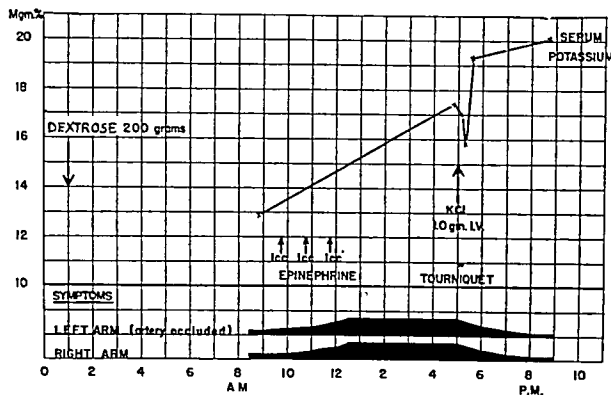


Chart 8.—Attack induced by dextrose and epinephrine. Potassium chloride injected into the right brachial vein. Note recovery of left arm despite arterial occlusion by tourniquet. The injected potassium rapidly disappeared from the blood serum. Serum potassium rose later during more complete recovery.

the defect? The distribution of paralysis and the loss of electrical excitability of the muscles pointed to a fault in the muscles themselves. On one occasion 20 cc. of potassium chloride in 0.5 per cent solution was injected into the left brachial artery while the venous return was obstructed for eight minutes by a blood pressure cuff inflated to 60 mm. of mercury to confine the potassium to the limb. Severe pain and intense vasoconstriction followed by flushing showed that the potassium had spread throughout the limb, but there was no recovery of power in the muscles. This amount of potassium chloride (0.1 Gm.) was theoretically sufficient to cause some local recovery, since as little as 0.5 Gm. had caused general improvement when injected intravenously in previous attacks. A negative result was obtained another time when 0.05 Gm. of potassium chloride was injected into the femoral artery.

These results suggested that the curative action of potassium was central or that some other substance was formed in the viscera by the action of potassium and thence carried to the muscles to restore their contractility. This led to the trial of certain choline esters as previously described. Intra-arterial injection of these substances caused no local recovery of power in the injected limb but when they entered the general circulation prompt recovery occurred throughout the body. We have no explanation at present for this action of the choline esters unless perhaps they stimulate some organ or tissue to release stored potassium.

From the following experiment (chart 8), which has been repeated three times with similar result, we are forced to conclude that the defect responsible for paralysis lies in the central nervous system: The arterial supply to one arm was occluded for from thirteen to seventeen minutes by a blood pressure cuff inflated to 200 mm. of mercury, while potassium chloride (50 cc. of a 2 per cent solution) was injected rapidly into the vein of the opposite arm. Movement began to return



in about five minutes in all limbs and recovery was as rapid in the still occluded limb as in the others. In other words, recovery occurred in a limb which was completely isolated from the rest of the body as regards humoral channels. These observations indicate that the defect is neurogenic. We have no explanation for the loss of direct electrical excitability of the muscles on this basis.

## COMMENT

In the patient with familial periodic paralysis the relationship of paralysis to reduction of serum potassium is clear but there is no indication of why the change comes about. It seems likely that potassium leaves the blood stream to supply a demand of the tissues. Excess of potassium in nerve or muscle is probably not responsible for paralysis, since administration of potassium is remedial. Nor is the low level of serum potassium the essential factor, since considerable partial recovery may occur after administration of potassium while the serum level as yet shows no elevation. When potassium is administered it may restore the excitability of nerve or muscle or it may act as intermediary for the production of some other substance which is capable of doing so. Our experiments indicate that the remedial effect is on the central nervous system and not on the muscle directly. Spontaneous recovery or that following administration of choline esters suggests that some organ or tissue is capable of releasing sufficient potassium to rectify the needs of the inexcitable nerve or muscle and also to raise the serum level to normal.

The experiments of Allott and McArdle<sup>10</sup> indicate that in addition to undue lability of serum potassium some abnormality of the neuromuscular mechanism is present in this disease. They have succeeded in reducing the serum potassium to 10.5 mg. per hundred cubic centimeters in normal persons and have observed a level as low as 7.6 mg. in one person. In no instance was there paralysis. There is support for this in the abnormality of creatine metabolism described by Ferrebee, Atchley and Loeb<sup>9</sup> and by us. In our case there was persistent creatinuria even between attacks, and creatinine excretion was variable. Allott and McArdle found alterations of phosphorus metabolism paralleling those of potassium, and Milhorat<sup>17</sup> noted a negative phosphorus balance following attacks.

The fact that family periodic paralysis has been found to be an inborn error of metabolism should stimulate work on other hereditary diseases of the neuromuscular system which are at present looked on with such pessimism. It is of interest that the distribution of affected muscles in this disease is the opposite of that in myasthenia gravis and is similar to that seen in the myopathies. Biemond and Daniels<sup>7</sup> observed that in some patients with familial periodic paralysis an atrophy of the muscles most affected by paralysis developed in later life.

It is possible too that the condition may exist in minor forms which do not lead to complete paralysis. Shinosaki<sup>4</sup> was of the opinion that attacks of sudden weakness in the legs occurring in some patients with exophthalmic goiter (so-called Basedow's paraplegia) were minor examples of periodic paralysis. In view of the effect of insulin on serum potassium it would also seem advisable to test this possible mechanism in the

rare monoplegias and other neurologic phenomena which do not respond to dextrose in cases of insulin shock. With the cooperation of Dr. T. E. Dancy we have determined the serum potassium in four patients receiving shock treatment for schizophrenia. Blood was taken before administration of insulin and again after from one and one-half to two hours of hypoglycemic coma. There was no significant change in serum potassium. These were patients, however, who recovered rapidly after the administration of dextrose and there were no persisting neurologic defects.

It is not possible to say whether the abnormality of potassium metabolism is peculiar to this disease or whether it is an exaggeration of a normal mechanism. Sodium metabolism appears to be unaffected and the defect is therefore unlike that of adrenal cortical activity.

The age incidence of the disease, its periodic character and its relation to thyroid activity all suggest an endocrine upset. At present, however, no gland or hormone is known to have so direct a relationship to potassium metabolism, and the primary cause of the disease must await further investigation.

## SUMMARY

1. In a classic case of familial periodic paralysis, attacks were associated with a marked fall of serum potassium. During recovery the serum potassium rose to normal.

2. Administration of potassium caused rapid disappearance of paralysis. Acetyl- $\beta$ -methylcholine chloride (mecholy) and choline chloride carbamate (doryl) also brought about recovery, although no potassium was administered. Prophylactic doses of potassium have prevented the occurrence of attacks.

3. Attacks were induced by the ingestion of large amounts of dextrose, with or without insulin, and by the administration of epinephrine or ephedrine.

4. Paralysis was not associated with a loss of potassium from the body. There was, however, a redistribution in which potassium was drained from the serum presumably to meet the needs of the tissues. No significant change occurred in the concentration of sodium or other important electrolytes in the blood.

5. Persistent creatinuria was present during attacks and in the intervals. Creatinine excretion in the urine was highly variable.

6. Experiments have indicated that the chemical defect responsible for paralysis lies in the central nervous system and not in the muscles.

7. Familial periodic paralysis is an inborn error of metabolism.

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**Hobbies.**—A profession cannot occupy all of one's time—or it ought not to—lest one become lopsided. Hobbies fill a gap in the lives of those who are most well rounded and promise equal satisfactions for less complete lives. . . . If you can grow, if you can relax, if you can be stimulated and refreshed by your hobby-tonic, you probably have found the right one. If you have not yet found it, begin thinking about it now, remembering meanwhile that Omnipotence of Thought isn't as efficacious as it once was, and that the surest way to develop an interest in a hobby is not by thinking about it but by doing something about it. You may be surprised how far it will take you. Hobbies cannot be developed on command. They develop by stages and are truly an expression of your very self.—Anderson, Camilla M.: *Emotional Hygiene*, Philadelphia, J. B. Lippincott Company, 1937.

17. Milhorat, A. T.: The Metabolism of Phosphorus in Periodic Family Paralysis, *J. Clin. Investigation* 16: 676 (July) 1937.

STUDIES ON THE MECHANISM OF  
THE ACTION OF SULFANILAMIDEI. THE BEARING OF THE CHARACTER OF  
THE LESION ON THE EFFECTIVENESS  
OF THE DRUG

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NEW YORK

The original observations of Domagk<sup>1</sup> on experimental mouse peritonitis and the clinical observations reported by Schreus<sup>2</sup> using prontosil (the disodium salt of 4-sulfamido-phenyl-2'-azo-7'-acetylamino-1'-hydroxynaphthalene-3',6' disulfonic acid) in the treatment of erysipelas led to the present investigations in April 1935. We have been interested, first, in evaluating the effectiveness and the limitations of this chemotherapeutic agent and its derivatives; second, in determining its mode of action, and, third, in throwing light on the biology of the hemolytic streptococcus. During the course of this study an increasing number of clinical reports have appeared; the effectiveness of sulfanilamide in certain infections needs no confirmation. The present report concerns itself primarily with an attempt to determine the mode of action on a number of bacterial infections encountered in a general hospital.

The published reports on the mode of action of sulfanilamide have in most instances dealt with observations in vitro or with a single type of experimental infection, peritonitis in the mouse,<sup>3</sup> and empyema in the rabbit.<sup>4</sup> Recently Osgood has added observations on culture of bone marrow.<sup>5</sup> It seemed to us that a study of the drug's effect on various types of hemolytic streptococcus diseases as they occur in man might lead to a hypothesis which could then be subjected to experimental tests. In this report the observations are chiefly clinical. Further experiments on the action of sulfanilamide in vitro will be reported shortly by one of us (J. S. L.).

## GENERAL PROCEDURE

The present observations are drawn from the first 250 patients (1936 and 1937) treated with sulfanilamide in the various services of the Presbyterian Hospital-Columbia University Medical Center and Willard Parker Hospital. Each infection was identified bacteriologically. Each patient was seen daily by at least two of us. Sulfanilamide levels of the blood were followed in most cases. The dosage was regulated to maintain in the blood a minimum level of 50 micrograms when practicable. Uncombined sulfanilamide was quantitatively determined in the blood and

other body fluids according to the method of Fuller.<sup>6</sup> Colorimetric comparisons against known standards were made in a staphophotometer, color filter 530 being used. The drug was administered at intervals of either four or six hours, chiefly by mouth. Infections treated included those caused by the hemolytic streptococcus, meningococcus, gonococcus, *Streptococcus viridans* and pneumococcus. The diseases treated in the order of frequency were scarlet fever, tonsillitis, sinusitis, otitis, mastoiditis, lymphangitis, erysipelas, pneumonia, bacteremia, endocarditis, primary peritonitis, lymphadenitis, chronic surgical infections with draining sinuses, early abscess formation, cellulitis, infected diabetic gangrene, meningitis, puerperal fever and cutaneous infections.

TOXICITY OF SULFANILAMIDE: NO RELATION TO  
THERAPEUTIC EFFECT

At the beginning of this study the only toxic effect that had been reported was cyanosis.<sup>7</sup> We soon encountered a great many other toxic manifestations. Many of these have since been reported by other observers. All symptoms and signs referable to sulfanilamide toxicity were carefully recorded and an attempt was made to determine their possible relation to the effectiveness of the drug. Approximately half of the adults and one fifth of the children showed some toxic manifestations. Some of these have been mild and others alarming; however, none of the five deaths in this series of 250 cases resulted from drug toxicity. The toxic manifestations observed were (a) mild—cyanosis, symptoms of the gastrointestinal tract and of the central nervous system, fever, precordial and abdominal pain, and acidosis; (b) severe—rash, jaundice, anemia, hemoglobinuria, and granulocytopenia; (c) secondary reactions and late manifestations.

## MILD MANIFESTATIONS

A. Cyanosis.—The development of cyanosis in patients receiving sulfanilamide has been a common occurrence. It was noted in approximately 50 per cent of adults and 20 per cent of children in whom the drug was used. This manifestation usually began with pallor and progressed to deep cyanosis, especially marked in the lips. In some persons cyanosis developed within twelve hours; most persons became blue before the third day of drug therapy. The intensity of the color seems to depend on the amount of drug in the circulation rather than on the amount of drug administered; it was paralleled closely by the concentration of methemoglobin in the blood as measured by the spectrophotometer (an illustrative case is given in the table). Cyanosis was detectable when the methemoglobin of the blood reached a concentration of 5 per cent and was striking at about 15 per cent. The highest value obtained was about 25 per cent in extreme cyanosis. Even at these levels there were no symptoms attributable to the methemoglobinemia per se. This manifestation did not seem to be dangerous in most cases, since it disappeared rapidly following withdrawal of the drug. However, in patients with diseases accompanied by lowered arterial oxygen, either systemically or in a localized area, the question arises whether the development of methemoglobinemia may aggravate the underlying disease. This problem has presented itself in pneumonia, in cardiac insufficiency and in recovery of compromised tissues following local inflammation or injury.

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4. Gay, F. P., and Clarke, A. R.: *J. Exper. Med.* **66**: 535 (Nov.) 1937.

5. Osgood, E. E.: Culture of Human Marrow, *J. A. M. A.* **110**: 349 (Jan. 29) 1938.

6. Fuller, A. T.: *Lancet* **1**: 194 (Jan. 23) 1937.

7. Colebrook and Kenny.<sup>3</sup>

**B. Gastrointestinal Symptoms.**—A great many disturbances in physiology of the gastrointestinal tract have occurred, especially among adults. Particularly frequent have been anorexia, nausea, vomiting and abdominal pain. Diarrhea has been severe in a few cases. Like cyanosis, these symptoms have disappeared rapidly when sulfanilamide therapy has been discontinued. This problem has been particularly acute in infants, in whom essential maintenance of nutrition has been made difficult by the severe anorexia, and persistent regurgitation has sometimes been displayed.

**C. Disturbances of the Central Nervous System.**—Dizziness and headache have been fairly common symptoms of sulfanilamide toxicity among adults. Mild personality changes, especially lightheadedness and depression, have been noted in many persons shortly after beginning the drug. A few have become disoriented and even manic.

All these symptoms have subsided rapidly when drug therapy was stopped. In cases in which the condition of the patient demanded, the drug has been continued

Observations on Patient B. Z. (History in Text)

Date	Sulfanilamide, Gm.	Cyanosis	Per Cent Methemoglobin	Serum Sulfanilamide, Micrograms per Cc.	Hemoglobin per 100 Cc. Blood
3/2	1.4	0	..	..	.....
3/3	4.4	++++	..	..	.....
3/4	3.8	++++	17	70	12 Gm.
3/5	3.0	++	16.5	..	.....
3/6	3.0	++	16	..	.....
3/7	3.0	++	..	..	.....
3/8	3.0	++	13	..	.....
3/9	3.0	++	..	..	.....
3/10	3.0	++	9	40	.....
3/11	3.0	++	..	..	.....
3/12	3.0	++	9	22	.....
3/13	2.6	++	..	..	.....
3/14	2.6	+	..	..	.....
3/15	2.6	+	6	20	.....
3/16	2.6	+	..	..	.....
3/17	2.6	+	..	..	.....
3/18	2.6	++	..	..	.....
3/19	2.6	++	4	20	.....
3/20	2.6	++	..	..	.....
3/21	2.6	++	..	..	.....
3/22	2.6	++	..	..	.....
3/23	2.6	++	4	..	.....
3/24	2.6	++	Trace	20	9.6 Gm.

in spite of the appearance of the aforementioned mild manifestations of toxicity. Reduction of the dosage by 25 per cent has generally sufficed to prevent the development of more severe symptoms.

**D. Sulfanilamide Fever.**—The development of drug fever has been an especially puzzling problem. This manifestation, rare in children, has been a frequent occurrence in adults. Most persons in whom sulfanilamide fever developed experienced some of the symptoms mentioned along with the appearance of pyrexia. A few, however, had pyrexia without symptoms. We have seen three different types of febrile response to sulfanilamide. The most common of these was a slowly rising temperature, occurring after the fourth day of therapy, progressing by stages each day (up to 106 F. in some instances) and falling about twenty-four hours after the drug was stopped. In some cases the temperature became normal within twenty-four hours but in most instances after forty-eight hours. In a smaller group of patients high fever and chills developed about twenty-four hours after the institution of therapy. These patients seemed to have a low tolerance for sulfanilamide. A few who had previously experienced sulfanilamide sickness showed a "hypersensitive reaction" on subsequent administrations of the drug from one month to one year later. As little as 0.6 Gm.

of the drug given to these "hypersensitive" subjects was sufficient to produce profound reactions within six hours, characterized by aches, chills, temperature spiking to 104 F., headache and leukocytosis as high as 30,000 per cubic millimeter.

**E. Precordial and Abdominal Pain.**—A few patients showed unexplained abdominal pains during the course of treatment, located chiefly in the upper quadrants. This occurred mainly in patients who were showing other evidence of toxicity from the drug, such as cyanosis or gastrointestinal complaints.

**F. Acidosis.**—One severe case of acidosis occurred in this series. Cessation of drug therapy was followed by prompt recovery.

None of the toxic manifestations discussed up to this point has seriously affected the outcome of the disease. Less frequent but much more severe are the following drug manifestations:

#### SEVERE MANIFESTATIONS

**A. Rash.**—In eight patients a maculopapular rash developed during or just after sulfanilamide therapy. The appearance was similar in all cases, resembling confluent measles. Any part or at times the entire body was involved. Itching was severe in some cases. The drug was stopped in each instance at the onset of rash because of the fear that continued sulfanilamide therapy might result in severe exfoliative dermatitis. The rash usually persisted for two days or longer, finally clearing completely.

**B. Jaundice.**—Two types of jaundice appeared; one a severe hemolytic jaundice, the other presumably a result of hepatitis. Although the jaundice subsided when the drug was discontinued, transfusions were necessary in some cases. Jaundice has been an extremely disturbing development; in view of the possibility of permanent damage to the liver, sulfanilamide was discontinued whenever it appeared. The jaundice was usually accompanied by secondary anemia.

**C. Anemia.**—Mild anemias developed in a number of cases, but it was not possible to determine with certainty whether they were due to the infection or to the drug. In a few patients, however, a severe hemolytic anemia seemed attributable to sulfanilamide. This occurred after only moderate dosage of the drug. The most intense were accompanied by icterus, the less severe by progressive anemia. In one case a large spleen and liver developed which subsided after transfusion and discontinuance of the drug. Transfusions were employed freely in anemia and seemed to counteract progression to some extent.

**D. Hemoglobinuria.**—In two patients on moderate doses of the drug hemoglobinuria developed shortly after sulfanilamide therapy was instituted. In one of these cases there was an alarming drop in the hemoglobin level.

**E. Granulocytopenia.**—Two patients, both females, had a depression of leukocytes following sulfanilamide therapy. In both these cases the infection may have been largely responsible for the granulocytopenia, and the part played by the drug cannot be accurately determined. In one instance the granulocytes disappeared completely and an alarming pyrexia developed. In both cases the final outcome was satisfactory.

#### SECONDARY REACTION: LATE MANIFESTATIONS

The drug symptoms mentioned up to this point usually appeared during the course of therapy. In one man severe sulfanilamide manifestations developed

eighteen days after the drug had been stopped, including pyrexia of 105 F., jaundice, enlargement of the spleen and liver, and a rash. It seemed perfectly definite that this patient had severe sulfanilamide sickness with hemolytic jaundice. The unusual feature was its appearance more than two weeks after the last dose of the drug.

The foregoing evidences of drug toxicity bore no observable relation to the effectiveness of sulfanilamide in overcoming infection. In some of the patients who showed marked toxic effects, the underlying infection seemed to be checked by the drug and promptly flared when the drug was discontinued. On the other hand, some patients who had toxic symptoms, such as severe cyanosis, were not benefited. The chief importance of the drug symptoms was their limiting effect on the amount of sulfanilamide that could be given. As far as the effect of sulfanilamide on the infectious agent was concerned, the presence or absence of symptoms of drug toxicity was irrelevant.

#### SEROLOGIC TYPE OF HEMOLYTIC STREPTOCOCCUS: NO RELATION TO EFFECTIVENESS OF SULFANILAMIDE THERAPY

It was not known whether all serologic types of hemolytic streptococci could be influenced by sulfanilamide or whether some were refractory to this drug. Daily cultures of the infected sites were made in most patients before, during and after chemotherapy was instituted. The organisms were typed according to the method described by Griffith.<sup>8</sup> Of the known types of hemolytic streptococci of group A, all but four were represented in this series. It was not possible to correlate the effectiveness of the therapy with the serologic type. No type seemed refractory to the drug. Moreover, human infections with organisms of Lancefield's groups C and G as well as group A seemed to be influenced by sulfanilamide therapy.

#### THE PROBLEM OF RELAPSE FOLLOWING WITH- DRAWAL OF SULFANILAMIDE

The administration of sulfanilamide was followed in a high proportion of cases by the disappearance of the infectious agent from cultures and the subsidence of signs and symptoms. The infecting organism had apparently been destroyed. In many hemolytic streptococcus infections, however, organisms which had disappeared during the course of treatment reappeared in predominance or even in pure culture within seventy-two hours of the time the drug was stopped. In most instances this was of no clinical importance. In a number of patients, however, the reappearance of the organism was accompanied by relapse. This occurred mostly in patients who had received the drug for less than ten days.<sup>9</sup> It was also noted that relapses were more common in some diseases than in others. They were frequent in patients with localized infections containing necrotic tissue, such as mastoiditis and abscesses, whereas in bacteremia and erysipelas they were not encountered. A few illustrative examples are given:

*Reappearance of Organism Without Symptoms.*—Many patients whose cultures had become negative for hemolytic streptococci had a reappearance of organisms of the same serologic type in almost pure culture

at the site of infection within three days after the drug had been stopped. This was particularly common in cases of acute pharyngitis and tonsillitis. In the majority of them convalescence proceeded uneventfully without return of fever or symptoms.

E. S., a boy aged 12 years, with mild scarlet fever, was given 2.5 Gm. of sulfanilamide a day for four and a half days. Culture on admission of material from the throat yielded predominantly the hemolytic streptococcus. Succeeding cultures showed the organism in decreasing numbers. After medication was stopped, the organisms began to increase rapidly. A week after the drug was stopped the hemolytic streptococcus was again predominant, and there was a mild temperature rise to 100.4 F. without symptoms.

*Reappearance of the Organism with Mild Symptoms.*—Some patients who showed a return of the infectious agent experienced mild symptoms of the same character but less severe than the original disease. These symptoms usually disappeared without administration of sulfanilamide being resumed. This was especially common in persons with throat infections but occurred also in other types of infections.

M. S., a woman aged 20, a student nurse with severe hemolytic streptococcus pharyngitis, was given sulfanilamide 4 Gm. for three days and 3 Gm. for two days. Culture of material from the throat the day medication was begun showed hemolytic streptococcus, type 13, predominating. Culture the day after medication was negative for the hemolytic streptococcus and continued so for a week. There was marked subjective improvement with a drop in temperature on the day following medication (perhaps coincident with rupture of an intratonsillar abscess). The patient was discharged from the hospital ten days after medication was stopped. On the same evening she had a recurrence of tonsillitis with cervical adenitis and a slight rise in temperature. Culture of material from the throat again yielded hemolytic streptococcus, type 13, predominantly.

*Recurrence of Severe Disease.*—In other patients a moderately severe disease picture developed, not unlike the original symptoms, when the drug was discontinued.

J. C., a woman aged 37, was admitted with chronic otitis and mastoiditis. Culture showed the hemolytic streptococcus. After four days in the hospital the temperature rose to 103 F. and frank signs of erysipelas developed about the ear. Sulfanilamide 4 Gm. a day was given and she showed marked improvement. The erysipelas disappeared and the temperature returned to normal. One week later she was being prepared for mastoidectomy and sulfanilamide was discontinued. After three days without the drug there was a recurrence of the erysipeloid lesion, mild fever, followed by edema of the eyelids and pain around the edge of the lesion. Sulfanilamide was again administered in the same doses and the response was similar to the original response; i. e., the temperature and cutaneous lesions disappeared in three days. The drug was continued, however, for nearly two weeks, at the end of which time no further relapse occurred.

The following cases show that patients with purulent lesions require a long course of therapy, owing to the survival of organisms in foci. In this group permanent clinical recovery seemed to depend on the development of adequate normal defenses. When this occurred, symptoms disappeared permanently, even in cases in which the individual remained a carrier of the infecting agent.

The first patient with a uterine infection required two weeks of chemotherapy before she was able to control the invasiveness of a virulent organism without the assistance of the drug.

M. C., a woman, had a postpartum infection, with a fever of 104 F. Vaginal culture showed the hemolytic streptococcus, group A, type 13, in pure culture. She was given sulfanilamide

8. Griffith, F.: J. Hyg. 34: 542 (Dec.) 1934.

9. The procedure subsequently adopted to prevent relapses has been to diminish the dose gradually over a period of days, the temperature curve being used as an index of controlled infection. Secondary courses of therapy were employed only when absolutely necessary, because of the greater incidence of severe toxic reactions in such cases.

2 Gm. the first day, and then 4 Gm. each day for one week. The temperature fell to normal within thirty-six hours. The sulfanilamide level of the blood at that time was about 30 micrograms per cubic centimeter. After one week the dosage was diminished to 2.6 Gm. Coincident with this the temperature rose, severe symptoms returned and cultures of material from the vagina became strongly positive with type 13. It was then necessary to increase the drug to the point of toxicity. The cultures of material from the vagina again became free of streptococcus when the sulfanilamide level in the blood reached 50 micrograms. After two weeks of therapy it was possible to discontinue the drug without untoward symptoms, although the patient remained a carrier for a period of months.

The next history likewise illustrates the necessity of maintaining a high level of sulfanilamide in the blood until natural resistance has had time to develop:

H. M., a young woman, was admitted to the hospital because of chills, fever and red and painful legs of twenty-nine hours' duration. On admission, the temperature was 105 F. and she showed massive edema with redness of the lower extremities and slight edema of the hands and face. There were large irregular tender blisters over the surface of the legs. It was felt that she had hemolytic streptococcus cellulitis, probably with infection of the blood stream, and sulfanilamide therapy was begun immediately. Blood culture on admission showed the hemolytic streptococcus in two flasks. Twenty-four hours after treatment the blood stream became sterile. However, cultures of the necrotic lesions on the legs were positive on the fourth day, when the blood contained 40 micrograms of sulfanilamide per cubic centimeter. The dosage was lowered on the eighth day. Three days later the temperature rose as the alarming symptoms returned and the dosage was again increased with prompt effect. It was possible to discontinue the drug during the fourth week without untoward results, although she remained a carrier.

So far as could be determined, sulfanilamide did not depress the development of the normal defense mechanism; but drug therapy was needed until the time of this development.

#### DEVELOPMENT OF METASTATIC LESIONS AND BACTEREMIA

In several patients hemolytic streptococcus metastatic lesions developed after the course of sulfanilamide therapy had been terminated, at a time when recovery was believed to be complete. In others hemolytic streptococcus bacteremia developed about thirty-six hours after the drug had been either stopped or markedly diminished in amount. In these cases the reduction in dose was prompted by the onset of mild toxic manifestations; the consequences of withdrawal were almost disastrous.

C. D., a girl aged 7 years, admitted with scarlet fever and signs of acute mastoiditis, was given sulfanilamide approximately from 2 to 3 Gm. each day. The temperature, which was 107 F. on admission, subsided slowly, keeping a range of about 100 to 101 F. In preparation for mastoidectomy, the dosage was lowered. Following mastoidectomy, the temperature rose markedly, reaching a height of from 105 to 106 F. Blood culture taken at this time showed hemolytic streptococcus of type 5, the same as the organisms recovered from the ears and throat on admission to the hospital. Sulfanilamide therapy was again started in similar doses and subsequent blood cultures all remained sterile. The temperature, however, spiked to from 103 to 104 F. for a number of days, and the patient remained acutely ill for two weeks following bacteremia. Eventually, on sulfanilamide therapy, the temperature subsided, and the patient was discharged fifty days after admission. This accident, almost fatal, followed the discontinuance of the drug.

These observations suggested that the protective action of sulfanilamide was greatest in the circulating fluids and that, after withdrawal, bacteria remaining in necrotic tissues could become highly invasive.

#### THE RELATION OF FREE SURGICAL DRAINAGE TO THE EFFECTIVENESS OF SULFANIL- AMIDE THERAPY

So far as could be determined, sulfanilamide was of no therapeutic value against well developed abscesses. In these cases surgical drainage later brought prompt relief.

We have encountered several chronic streptococcal infections refractory to surgical treatment in which the natural defense mechanism was not capable of preventing the occasional migration of organisms to new tissue. There was little immediate risk of generalized blood or lymphatic invasion, yet the antibacterial forces were not strong enough to overcome the infection. We present two cases of this type in which sulfanilamide proved highly effective. In the first case, one of long duration, the drug was continued well beyond the stage of healing, and the result was completely satisfactory, at least as far as one can judge from the follow-up period of eighteen months. In the second case, premature withdrawal of the drug following an initial satisfactory response was followed by the reappearance of streptococci in the exudates and a simultaneous flare-up in the activity of the local infection. Resumption of sulfanilamide therapy eventually cleared this infection.

M. S., a school girl aged 15 years, first admitted to the private pavilion under the care of Dr. Auchincloss Jan. 9, 1931, had had hemolytic streptococcus septicemia eleven months before, followed by pneumonia and suppurative arthritis of the right sacro-iliac joint. The latter had drained spontaneously at the right pelvic brim seven months before, and the discharge had continued intermittently ever since, inadequate drainage producing periodic spikes of fever.

Over a period of sixty-eight months, the patient continued to have almost constant suppuration in the pelvis. She had twenty-six operations during that time. It was found that constant maintenance of free drainage both anteriorly and posteriorly was essential in order to prevent the formation of new abscesses. The process later invaded the uterovesical space and produced an anterior vesical fistula, which finally closed. She either had drainage tubes constantly in place to prevent closure and backing up of pus, or else her ambulatory period was of short duration, an early recurrence of pain and fever bringing her back to the hospital.

Her last operation was on Oct. 13, 1936, when simple excision of a granulating tract in the lower anterior wall of the abdomen was done. Following the immediate postoperative period, her temperature became normal, but she continued to have fairly profuse drainage from each of three tracts, cultures showing the same type 13 (Griffith) hemolytic streptococcus which had constantly occurred in almost pure culture in her discharges.

Sulfanilamide 3 Gm. daily was started October 27 and continued until discharge November 23. The draining sinuses were irrigated with a 1.2 per cent solution of sulfanilamide in 0.5 per cent saline solution. The discharge diminished rapidly in amount after treatment was started and became thin and sticky, the granulations lining the sinuses assumed a healthy appearance, and the sinuses filled in rapidly from the depths. It appeared on purely clinical grounds to Dr. Auchincloss, who had had the patient under almost constant observation for five and a half years, that a type of healing was taking place which he had never observed in this patient's wounds. A follow-up period of eighteen months has now passed without any evidence of recurrent disease. After discharge from the hospital, she continued to take from 1 to 2 Gm. of sulfanilamide daily for about one month. At no time were serious symptoms or signs of toxicity noted.

L. B., a woman aged 26, a telephone operator, complained of ulceration of the pectoral region for ten months. At that time an abscess had developed in the right breast which had been incised and drained but failed to heal. Spreading and undermining continued in spite of repeated surgical procedures in

several hospitals. The patient had had some fever most of the time and a great deal of pain. On examination the patient was emaciated with extensive ulceration of the right pectoral region, the right breast being attached by only a short pedicle of skin beneath the clavicle. There was undermining of the skin peripheral to the ulcer, and three "daughter ulcers" had formed in the pectoral and infraclavicular regions. Exudate was profuse and foul. Cultures showed hemolytic streptococci.

With no operative intervention the patient was started on sulfanilamide 4.5 Gm. daily. After nine days the cultures showed no hemolytic streptococci and marked clinical improvement had occurred, so that the drug was stopped when the patient became nauseated. After six days without sulfanilamide there was an increase in the amount of discharge, the wound looked worse and cultures showed reappearance of streptococci. The drug was resumed and rapid improvement again occurred, although this time the disappearance of the hemolytic streptococci from the wound was slowed. During the next twelve weeks she continued to receive sulfanilamide, though most of the time the usual daily dose was only 2.5 Gm. During the fourteen weeks of hospitalization it was possible to perform a plastic operation, with excision of contracted scar tissue and resuture of the breast to the chest wall. This healed uneventfully and the patient was discharged.

Both of these chronic infections were treated successfully. In the presence of sulfanilamide the organisms were unable to form metastatic lesions. Free surgical drainage permitted elimination of pus. The combined treatment gradually eliminated the organisms, which had persisted deep in the wounds for a long time. In the first of these cases most of the necrotic tissue which might have served as a protected nidus for persistent infections had been surgically removed. In the second case there was little deep necrosis when treatment was started.

#### THE RELATION OF MIXED INFECTIONS TO THE EFFECTIVENESS OF SULFANILAMIDE THERAPY

In necrotic lesions in which both hemolytic streptococci and hemolytic staphylococci occurred, drug therapy was often ineffective even in the presence of free surgical drainage. The staphylococci in local lesions were not influenced by sulfanilamide. The continuation of purulent lesions with this organism seemed to inhibit the chemotherapeutic effect of sulfanilamide on hemolytic streptococci.

A. McL., a housewife aged 37, had an indolent infection of the interphalangeal joint of the left thumb which was observed for several days in the outpatient department. She was finally admitted for incision and drainage, at which time cultures from the joint space showed hemolytic streptococci. Sulfanilamide was started on the fifth day after operation in order to see whether rapid elimination of the streptococci could be effected. On the seventh day *Staphylococcus aureus* as well as streptococci was found in the exudate, and these two organisms persisted in the wound for three weeks in spite of continued sulfanilamide. Little effect on the character of the lesion was obtained by local irrigation with sulfanilamide solution.

The possibility suggested itself that the staphylococcal activity created environmental conditions which interfered with the effect of sulfanilamide on the streptococcus.

#### THE EFFECT OF SULFANILAMIDE ON RAPIDLY SPREADING INFECTIONS

Sulfanilamide therapy seemed most effective in rapidly spreading lesions in which there had been little tissue destruction:

J. I., a man aged 31, an apartment house superintendent, was admitted with extensive cellulitis of the left hand twenty-four hours after introduction of a splinter of manila rope into

the middle finger. The temperature was 103 F. on admission. In spite of the very short time since the primary injury, there was a well developed pattern of lymphangitis extending to the shoulder. There was exquisite tenderness and swelling around the site of the splinter wound, but no signs of tenosynovitis were present. An exploration of the superficial layer of skin around the wound was made to see whether any foreign body was present, but incision of the closed spaces of the finger was not done because of the unlocalized character of the infection. Sulfanilamide was started, wet dressings and elevation were instituted and, within twenty-four hours, subsidence of spread of the lesion had definitely commenced. On the fifth day the temperature returned to normal. On that day, signs of localized abscess were noted and the middle closed space of the middle finger was incised. A small drop of pus was obtained which showed hemolytic streptococci. Further recovery and wound healing were uneventful. Blood cultures throughout were negative.

This patient recovered promptly from a dangerous infection. The therapeutic effect of the drug was striking in the newly invaded tissues; however, a small abscess which developed continued to yield viable organisms in spite of sulfanilamide therapy.

A second case illustrates the effectiveness of sulfanilamide in preventing invasion into the meninges and its inability to sterilize necrotic tissue:

C. S., a boy aged 4 years, was admitted to the Babies Hospital because of intermittent earache and headache for three weeks. On lying down he complained of pain in his head, which was relieved on sitting up. There was an extensive, soft, fluctuant, exquisitely tender swelling over the right parietal region over the occipital bone. The right tympanum was white and bulging posteriorly; surface vessels were prominent.

On the day of admission a right simple mastoidectomy was performed. Near the sinodural angle there was a collection of creamy pus. The dural plate and mastoid cells in this region were soft. Pus continued to appear in such a steady stream that it was necessary to remove an area of bone extending about an inch toward the occiput. The dura was shaggy, thickened and inflamed and the brain beneath was soft.

He stood the operation fairly well and was given a small transfusion afterward. The temperature reached 103 F. on the two following days. Culture of the pus from the epidural abscess showed a pure culture of hemolytic streptococcus. Sulfanilamide was begun on the second day after operation and continued for three weeks (2.5 Gm. a day).

On the fourth and fifth days he was afebrile, but the temperature began to rise at the end of the first week and continued elevated through the second week. A superficial incision at this time released more pus, and the temperature fell to normal. He continued afebrile during the fourth week, when sulfanilamide was stopped. He was discharged after six weeks.

At home he appeared to be well for a period of ten days, without fever or complaint. On the eleventh day he awoke at 1 a. m., feverish, complaining of headache. He was brought to the hospital and while in the clinic had a generalized convulsion lasting two minutes. He was readmitted with a temperature of 104 F. The previously operated area was explored for brain abscess; none was found. However, necrotic bone was removed from two sites; each contained a pure culture of the hemolytic streptococcus. Throughout the second admission he received 2.5 Gm. of sulfanilamide a day until the ninth week, when the dose was reduced to 2 Gm. He was discharged after nine weeks, having made a satisfactory recovery.

Sulfanilamide prevented further spreading of this dangerous infection but was unable to kill organisms in necrotic bone.

A third case shows that under some circumstances the use of sulfanilamide in a rapidly spreading lesion may lead to the formation of a sterile abscess:

B. Z., a school boy aged 16 years, was admitted with hemolytic streptococcus septicemia associated with pansinusitis. He was desperately ill, with a temperature of 105 F., and showed a diffuse cellulitis of the right temporal region. On the day of



admission signs of acute suppurative arthritis of the right shoulder developed. Under sulfanilamide therapy his blood became sterile within forty-eight hours. The signs of cellulitis of the temporal region subsided, leaving a localized, fluctuant area which, when opened, yielded sterile pus on repeated cultivation. The shoulder signs and symptoms disappeared without surgical intervention. The data are given in the accompanying table.

Sterile abscesses were found in two other patients treated with sulfanilamide. In all three cases treatment was instituted before localization had occurred. It appeared that sulfanilamide sterilized the lesions when administered before necrosis of the tissue had taken place.

Finally, another case illustrates the effectiveness of sulfanilamide in a rapidly spreading infection and its ineffectiveness in a localized lesion:

M. K., an infant aged 11 months, was admitted in the early stages of acute primary hemolytic streptococcus peritonitis with septicemia. Blood and abdominal paracentesis yielded a pure culture of the hemolytic streptococcus. Under sulfanilamide therapy the blood became sterile and the signs of peritonitis disappeared after one week. No localized peritoneal abscess formed.

During the second week a suppurative phlebitis developed around an infusion cannula in the saphenous vein, and coincident with this blood culture became positive. Because of suspected hepatitis, sulfanilamide was withheld for twenty-four hours and the colony count rose from 10 to 1,328 per cubic centimeter in the blood culture. Sulfanilamide therapy was resumed and an abscess which formed at the site of the phlebitis was drained. Examination of the pus showed hemolytic streptococcus in pure culture. The blood became sterile and remained so. Recovery was complete, and the patient has enjoyed good health during the follow-up period of fourteen months.

Sulfanilamide sterilized the blood stream and the peritoneal cavity in this critically ill infant. However, in the presence of traumatized tissue and hematoma formation sulfanilamide was unable to sterilize a localized infection. Organisms in this focus remained highly virulent but were unable to form metastatic lesions elsewhere in the presence of a high level of sulfanilamide in the blood.

#### SULFANILAMIDE THERAPY: NO EFFECT ON IMMUNE BODY FORMATION

That sulfanilamide may have toxic effects on the liver, spleen and bone marrow has been pointed out. Whether this drug might depress or stimulate antibody formation was unknown. To determine this, two types of studies were made.

The first of these consisted in serial determinations of antistreptolysin over a period of from thirty to sixty days after infection. This antibody to the streptococcus was examined because it permits quantitative measurement and because previous experience had indicated the normal curves in untreated infections. Samples of blood were obtained at intervals of from two to seven days, and the antibody curves for approximately 100 patients receiving sulfanilamide were determined. On the whole, the curves were similar to those of untreated patients.

The second study was made on guinea pigs. Serial determinations of antistreptolysin were made on animals given agar foci, inoculated with varying doses of hemolytic streptococcus, N Y 5 (0.0001, 0.1 and 0.5 cc. of eighteen hour broth cultures) and treated for varying periods (two, three and four weeks) with sulfanilamide (5 cc. of a 2 per cent solution twice daily). Thirty-two pigs were treated with sulfanilamide; eight

controls were untreated. The hemolytic streptococcus was recovered from the abscesses of all pigs but one. In the treated pigs that survived for two weeks after infection, antistreptolysin levels developed similar to those in the controls. One control pig failed to form the antibody. There was no indication that sulfanilamide had any effect on production of antistreptolysin.

#### COMMENT

The clinical aspects of this study showed striking differences in the effectiveness of sulfanilamide. These differences were related more to the character of the lesion than to the identity of the bacterial infection. Sulfanilamide was most effective in bacteremia, lymphangitis, erysipelas and cellulitis; it was highly effective in early infections with little suppuration. It had a questionable effect in scarlet fever, tonsillitis, sinusitis, otitis and mastoiditis. The drug was ineffective when abscesses were well established, except perhaps in limiting their further spread and protecting normal surrounding tissues against invasion when drainage was used.

So far as could be determined from scarlet fever, the drug had no effect on toxemia of streptococcal origin. It is possible, however, that the symptoms in these persons were due to toxin absorbed before sulfanilamide therapy was instituted. The majority of strains of hemolytic streptococci showed little change in their production of hemolysin following sulfanilamide therapy. In a few organisms, however, production of hemolysin was strikingly inhibited. It seemed to us that any depression in the production of soluble toxins was of secondary importance.

The striking effect of sulfanilamide was a depression of the invasive properties of the organism. This effect was definite within eighteen hours in the case of bacteria circulating in tissue fluids or in newly invaded tissues.

In contrast, the presence of debris, human or bacterial, diminished the effectiveness of sulfanilamide on the hemolytic streptococcus. In each instance the organisms remaining in broken down tissue maintained their virulence. It is not known whether the debris itself had a protective action on the organisms or whether there was insufficient penetration of the drug into the locus.

It seems possible that sulfanilamide may alter the total metabolism of the micro-organism or may interfere especially with some specific function, such as its capacity to digest protein. In either case the presence of necrotic tissues appears to be of great importance. Sulfanilamide should be considered an agent which supplements, and in no way supplants, antibacterial immunity. These aspects of the problem are now under experimental investigation by one of us (J. S. L.) and will be the subject of a forthcoming report.

#### CONCLUSIONS

The effectiveness of sulfanilamide therapy is related to the type of lesion.

The function of the micro-organism, which is strikingly depressed by sulfanilamide, is its capacity to invade tissue.

The effect of the drug on bacterial invasiveness seems to be influenced by the amount of debris present in the lesion.

These phenomena are being investigated experimentally to determine the mode of action of sulfanilamide.

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PSEUDOHYPERTROPHIC MUSCULAR  
DYSTROPHY

## AN EVALUATION OF RECENT STUDIES

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The treatment of pseudohypertrophic muscular dystrophy has passed through many cycles, depending on the prevailing theory of pathogenesis. Each has had a short period of usefulness which ended when failure to produce enduring clinical improvement made it no longer tenable. At present the myodystrophic patient will probably pass through the entire gamut of therapy, beginning with the more recent forms and working backward as each in turn is discarded as ineffective.

For a time all interest centered on endocrinologic factors,<sup>1</sup> and practically every gland was incriminated. The pineal and pituitary<sup>2</sup> glands were particularly singled out by many workers, who pointed to a similarity of symptoms in diseases of these ductless glands to those found in the dystrophic patient.

In medical writings repeated emphasis is placed on a supposed disturbance in carbohydrate metabolism.<sup>3</sup> These statements are based on chemical studies<sup>4</sup> and on deductions drawn from the occurrence of creatinuria in unrelated conditions such as diabetes and starvation.

Occasionally a sporadic case of pseudohypertrophic muscular dystrophy is reported occurring as a post-encephalitic residuum or following acute anterior poliomyelitis.<sup>5</sup> This has led some writers to hypothesize a lesion in a hypothalamic center.

In 1930 Kuré and Okinaka<sup>6</sup> began treating their patients with epinephrine and pilocarpine, basing their therapy on the belief that the disease had its origin in a lesion of the autonomic nervous system. They reported very encouraging results, varying from startling improvement to a retardation or halting of the progress of the disease.

Hough and others in this country followed along these lines and reported good results. Our experience with this form of therapy has been disappointing.

Beginning with the work of Milhorat, Techner and Thomas<sup>7</sup> in 1932, the literature was studded with enthusiastic reports on the use of aminoacetic acid in

the treatment of the primary myopathies, particularly pseudohypertrophic muscular dystrophy and myasthenia gravis. Along with Tripoli and Beard,<sup>8</sup> Boothby<sup>9</sup> and others, we too obtained encouraging results. As our experience with amino acid therapy progressed, however, it became apparent to us that the progress of the disease remained unaltered and that temporary improvement, if any, was short lived in the face of advancing atrophy and fibrosis.

Our interest was again revived on learning of the recent work of Meldolesi<sup>10</sup> in Italy, covering a period of nine years and based on more than 100 cases. The theory advanced by this worker is that the muscular dystrophies are caused by a primary disease affecting the pancreas, as a result of which tryptic and lipolytic digestive processes are markedly impaired. Failure of adequate protein absorption causes a depletion of protein reserves resulting in a dysplasia of striated muscle. This occurs in persons showing a hereditary and familial diathesis the basis of which is a lack of pigment of the muscles.

More specifically Meldolesi reported that the curves for the secretion of lipase, diastase and trypsin were delayed in their rise and did not reach normal levels. Many patients showed a diminished dextrose tolerance. The feces contained an increased amount of neutral fats and fatty acids. The urines showed a total excretion of nitrogen which was low and independent of the intake of protein before therapy was started and showed a rapid rise under treatment. Following the institution of therapy, creatinuria rapidly diminished until within a few weeks a negligible amount was excreted. Similarly the excretion of creatinine increased in a rapid progressive way until it made up almost the whole fraction of the total creatinine. Treatment was directed toward correcting the deficient digestion of protein and altered carbohydrate metabolism.

Meldolesi's treatment was essentially the administration of from 40 to 60 drops of pepsin-pancreatin (a product of Richter of Budapest) twice a day, insulin and intravenous dextrose.

In the present work we attempted to determine the soundness of several of Meldolesi's basic contentions, namely:

1. That these patients are unable to digest proteins because of a lack of or deficiency in their tryptic ferments.
2. That, because of this deficiency, excretion of urinary nitrogen is independent of variations in the intake of protein nitrogen.
3. That these patients have a disturbed carbohydrate metabolism as evidenced by a diminished tolerance for dextrose.
4. That creatinuria is progressively abolished following institution of therapy.

## MATERIAL AND PLAN FOR THIS STUDY

A small group of patients was admitted to the Max Pam Unit for Metabolic Research, where they could be studied intensively under controlled conditions. This seemed to us more desirable than ordinary hospitali-

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zation of a larger group, in which the amount of study would be necessarily restricted.

Five patients were selected, each of whom had been under observation for several years and had passed through the gamut of the more recent forms of therapy. Two of these patients were typical examples of the Duchenne type. Two belonged to the same group but presented a variant in the form of a superimposed Froelich's syndrome. The fifth also was of the Duchenne type but presented in addition a facial component such as occurs in the Landouzy-Dejerine type. The onset in each case occurred before or at about 6 years of age. Three patients were no longer ambulatory and the remaining two were markedly limited as to activity.

TABLE 1.—Dextrose Tolerance

Case	Fast- ing		30 Min.	60 Min.	90 Min.	120 Min.	150 Min.	180 Min.
1	79	25 Gm. of	369	...	135	...	56	...
2	85	dextrose	150	...	88	...	63	...
3	72	given intra-	118	85	...	56	...	66
4	59	venously	176	130	...	74	...	33

In cooperation with our metabolic unit it was proposed to determine on a quantitatively and qualitatively fixed diet:

1. The state of digestion, especially of proteins and fats, as indicated by examination of the stool.
2. The tryptic activity of the duodenal contents.
3. The daily excretion of nitrogen in the urine and its behavior with changes in the intake of nitrogen.
4. The dextrose tolerance.
5. The daily excretion of creatine and creatinine.
6. Variations in the foregoing data following therapy.
7. The clinical effect of therapy.

RESULTS AND ANALYSIS OF DATA

*Stool Examinations.*—In three of the five cases, stools on repeated examination were normal in gross appearance and microscopically. Muscle fibers, when present, were well digested, and fat globules could occasionally be demonstrated in a finely emulsified state with sudan III stain. In the remaining two cases the stools were unusual in the amount of grossly undigested material, which on microscopic examination, however, proved to be almost entirely vegetable in nature. There was no evidence, even in the latter cases, of disturbed digestion of meat or fat constituents of the food.

*Tryptic Activity of the Duodenal Contents.*—Successful intubation of the duodenum was performed in three of the five cases and determinations of tryptic activity made on the fasting contents and on the aspirations following stimulation with 20 cc. of twentieth normal hydrochloric acid.

We did not attempt to obtain prolonged secretory curves. A study of the aspirated contents of the duodenum convinced us that, unless aspiration by continuous suction of the gastric contents is maintained, dilution of the duodenal contents is sufficient to detract from the significance of a secretory curve. Therefore, normal values obtained at any period of the experiment were considered evidence of adequate secretion. Control values in normal children served as the basis for comparison.

In the second patient the fasting content showed normal tryptic activity. Specimens obtained thirty minutes and one hour later showed extremely low values.

The third patient showed normal initial values in both trypsin and lipase. Specimens one-half hour and one and one-half hours after introduction of twentieth normal hydrochloric acid gave tryptic values two and two and one-half times the initial level. Lipolytic activity maintained its fasting level.

*Dextrose Tolerance.*—This test was performed on four of the five patients, the intravenous method of administration of dextrose being used to obviate variations in results due to unknown factors of absorption. We used the Somogy modification of the Shaffer-Hartman method for true blood sugar. Normal limits for the fasting blood sugar level by this method are given as from 60 to 90 mg. per hundred cubic centimeters. The results are shown in table 1.

Fasting blood sugar levels of all four patients are well within normal limits. In all cases the ability to remove dextrose from the circulation does not appear to be impaired.

*Excretion of Nitrogen.*—Total excretion of nitrogen was determined in specimens of twenty-four hour urine collected under toluene under varying conditions of food intake. Results in one of the more advanced cases are shown in table 2 and are representative of the uniform response of the entire group.

It will be noted that the total excretion of nitrogen in the urine varies directly with the intake of protein.

On the various dietary regimens, which varied particularly as to protein and carbohydrate, each of the five patients consistently maintained a positive nitrogen balance.

*Excretion of Creatine and Creatinine.*—The effect of dietary variations on these urinary constituents was noted in daily specimens of twenty-four hour urine. The effect of changes in the intake of protein and of administration of large amounts of carbohydrate and insulin are noted in table 3.

From table 3 it can be seen that both creatine and, to a lesser extent, creatinine follow closely the curve of the excretion of nitrogen. Total nitrogen as in table 2 bears a direct relationship to the intake of

TABLE 2.—Excretion of Nitrogen

Date.....	12/7	12/8	12/11	12/10	12/20	12/21
Food Intake (Gm.)						
Protein.....	64	50	56	140	140	106
Fat.....	114	98	108	116	116	93
Carbohydrate.....	294	309	309	230	230	230
Total nitrogen in grams	6.32	4.99	4.78	14.12	13.86	11.66

protein. It is interesting to note that creatine and, to a lesser extent, creatinine, when expressed as percentage of total nitrogen, bear an inverse relationship to the latter. This will be discussed later.

*Effect of Pancreatin Therapy on Excretion of Creatine and Creatinine.*—The two patients showing some disturbance in digestion were selected for this experiment. One was treated for sixty-seven days and the other for forty-four days with a concentrated enteric coated pancreatin preparation.<sup>11</sup> The results in the latter patient are representative and are presented in table 4.

In neither patient did creatinuria tend to diminish with the administration of pancreatin. Its excretion was similar to that seen in table 3, in which experi-

11. Dr. David Klein of the Wilson Laboratories supplied the enteric coated pancreatin used in this study.

ment the patients received no pancreatin; i. e., it varied directly with urinary total nitrogen. Nor did the excretion of creatine compose a smaller fraction of the total creatinine.

*The Effect of Therapy as Judged Clinically.*—In estimating clinical results a quantitative expression of the patient's muscle power was sought. It seemed quite apparent from past experience that testimonial evidence from whatever source obtained was worthless. A series of test exercises involving the performance of definite coordinated muscle actions was therefore outlined for each patient, the ability of the patient to repeat them being noted. These quantitative figures served as an index of muscular endurance. Other test exercises were devised to determine the maximum initial performance. These records were obtained twice each week by the same trained physical therapist and were maintained for a period of nine months.

The clinical results following pancreatin therapy, administration of dextrose and insulin and of insulin alone, variations in diet from low protein to high protein and similar variations in intake of carbohydrate were evaluated on the basis of the curves obtained on tabulation of muscular performances.

When creatine and creatinine are expressed in terms of the percentage of total nitrogen excreted they bear an inverse relationship to the latter. Diminution in the intake of protein causes a fall in total excretion of nitrogen and that fraction of the latter which represents exogenous creatine and creatinine. Endogenous catabolism remaining the same, the excretion of creatine and creatinine derived from it makes up a disproportionate fraction of the total excretion of nitrogen and hence bears an inverse relationship to the latter in terms of percentage. This is most strikingly seen when the protein sparing action of large amounts of carbohydrate is involved.

For years it has been believed that there is in this disease a disturbance in glycogenesis, and on this thesis feeding of carbohydrate alone or with insulin have formed a part of the therapeutic regimen in many clinics. The striking manner in which administration of carbohydrates stops the creatinuria of starvation has been offered as corroborative evidence. In our chemical studies of the blood we cannot find support for these ideas nor have we noted any correlation of clinical improvement with periods of high ingestion of carbohydrate.

TABLE 3.—Excretion of Creatine and Creatinine

Date, 1938.....	1/5	1/6	1/9	1/15	1/29	1/30	1/31	2/1	4/4	4/5	4/6	4/7
Diet: Protein.....	48	47	49	48	88	100	87	86	34	49	49	39
Fat.....	74	74	82	74	47	61	50	48	52	52	60	42
Carbohydrate.....	164	171	163	169	150	151	160	160	230*	280*	278*	287*
Creatine (Gm.).....	0.623	0.681	0.776	0.665	0.896	0.760	0.989	1.015	0.602	0.779	0.746	0.664
Creatinine (Gm.).....	0.391	0.451	0.505	0.442	0.671	0.405	0.434	0.371	0.225	0.427	0.437	0.237
Total nitrogen (Gm.).....	5.29	5.18	9.05	5.13	12.34	8.25	10.96	11.06	2.95	5.88	5.71	3.48
Creatine percentage of total nitrogen.....	11.7	13.1	8.5	12.9	7.3	9.2	9.0	9.1	20.4	13.2	13.0	19.1
Creatinine percentage of total nitrogen.....	7.3	8.7	5.5	8.6	5.4	4.9	3.9	5.1	7.6	7.2	7.6	6.8

\* Values include 50 Gm. of dextrose-intravenously by slow drip.

All the patients studied showed a slow progressive improvement in their ability to perform the tests outlined. However, this improvement bore no apparent relationship to the institution of various forms of therapy, including pancreatin, nor did it decline when treatment ceased. Improvement was most marked in the muscle groups most affected by the disease.

COMMENT

It appears from the results of these experiments that the patient with pseudohypertrophic muscular dystrophy does not lack the ability to digest proteins or to transform these proteins into the end products of ferment activity. There is apparently no disturbance in the formation of creatine, as one can readily note from the definite and proportionate manner in which creatinuria follows nitrogenous intake. For a long time it was felt that both creatine and creatinine had their origin solely in endogenous metabolism,<sup>12</sup> but our results and those of other investigators<sup>13</sup> indicate that there must also exist an exogenous source. The myo-dystrophic patient is a better subject for the study of creatine metabolism than the normal person and in excretion of creatine is analogous to the diabetic patient as regards dextrose. Added proof of the dual origin of creatine is suggested in the analysis of table 3.

From a purely clinical standpoint it has been our experience that no form of therapy available at the present time acts in a specific way to halt the progress of this disease. The patients included in this report have shown definite improvement in their ability to perform their test exercises, but this progress could not be correlated with any specific form of therapy employed. Had treatment remained constant in nature we would have felt justified in claiming a certain

TABLE 4.—Effect of Pancreatin Therapy on Excretion of Creatine and Creatinine

	Period 1 (Av. 3 Days) Pancreatin- Low Protein	Period 2 (Av. 3 Days) Pancreatin- High Protein	Period 3 (Av. 3 Days) Pancreatin- Insulin 10 10-0
Protein intake (Gm.).....	60	129	108
Urinary nitrogen (Gm.).....	5.599	13.210	11.929
Creatine (Gm.).....	0.753	1.284	1.462
".....	0.251	0.422	0.267
".....	1.004	1.706	1.729
".....	3.4	5.7	3.6
".....	75	75	75

degree of success for it. We attribute the improvement in these patients to the prolonged period of hospitalization, which included adequate diets, and, what is perhaps more important, to the regulated daily routine and physical activity, including that involved in the performance of the test exercises. That regulated exercise is of importance was pointed out long ago and becomes apparent when one notes the harmful

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effect of restriction of activity such as follows biopsy of the gastrocnemius muscle. Such treatment, however, offers little of lasting value in the face of the seemingly inexorable inroads which this disease makes on the muscle.

What then is the path of the future? Recent work has taught us much of the physiology of muscle and has clarified some of the intricate mechanisms involved.<sup>14</sup> We know that creatine plays a vital part in the initiation of muscular contraction and that it occurs in loose combination with phosphorus. From a study of the chemistry of dystrophic muscles, Nevin<sup>15</sup> has shown that the usual breakdown of creatine-phosphoric acid does occur, differing but quantitatively from the normal. The ability to resynthesize this compound to its initial value also is retained. Differences are apparently quantitative rather than qualitative, and one is inclined to study more closely the known constituents of muscle to ascertain whether any substance is markedly deficient.

Such a deficiency has been noted clinically to exist in the coloring of the dystrophic muscle. Muscle pallor has been recently emphasized by Meldolesi.<sup>16</sup> This lack of adequate coloring led us to a review of the literature on muscle pigment and we found that the substance had been almost entirely forgotten in the study of the intricate processes which comprise the chemistry of muscle.

In 1887 MacMunn<sup>16</sup> described a number of tissue pigments, naming the one found in muscle myohematin. Gunther<sup>17</sup> in 1921 spoke of myoglobin and recognized that the pigment was not identical with hemoglobin. Kuhne<sup>18</sup> twenty years before MacMunn presented evidence to show that this muscle pigment had a respiratory function. More recently the study of this pigment has been carried on intensively and its isolation in animals has been accomplished by Theorrel<sup>19</sup> and later by Watson.<sup>20</sup>

As yet no place has been found for this substance in the economy of muscular contraction. It seems unlikely that nature has provided skeletal muscle with a substance which has tremendous oxidizing properties<sup>21</sup> (ten times that of hemoglobin) unless this substance plays an important role in the chemistry of muscular contraction. Eggleton<sup>22</sup> has shown that creatine diffuses rapidly from fatigued muscle and that this diffusion ceases when oxygen is supplied. In the lungs there is provided a delicate network of capillaries closely associated with specialized alveolar epithelium for gaseous exchange. In the muscle, where there must occur a rapid diffusion of oxygen from the capillaries, it would seem that a substance such as myoglobin would be essential. That myoglobin may indeed supply this mechanism has recently been shown by Millikan,<sup>23</sup> who by photoelectric spectroscopy has proved that it acts as a short-time oxygen store in the muscle to tide it over periods of oxygen want in each contraction.

We feel that when more is known of the place this pigment substance occupies in the economy of muscular

processes we shall have found an important clue to the treatment of the myodystrophic patient. Quantitative and qualitative studies of the myoglobin content of muscles in various pathologic states and their correlation with known facts of the chemistry of these muscles will be necessary to evaluate the clinical importance of myoglobin. Such studies are in progress.

#### SUMMARY AND CONCLUSIONS

1. Five patients with pseudohypertrophic muscular dystrophy were studied to determine whether a deficiency in the external secretion of the pancreas forms a part of the syndrome.
2. No evidence could be found from a study of the stools, duodenal contents and urine that the pancreas is involved.
3. Improvement while under observation was found to be unrelated to specific treatment.
4. It appears that muscle pigment or myoglobin is of importance in the economy of muscular processes.

### THE TREATMENT OF CARDIAC IRREGULARITIES

GEORGE FAHR, M.D.

MINNEAPOLIS

One of the most experienced cardiologists<sup>1</sup> has estimated that serious cardiac failure is accompanied by auricular fibrillation in more than half the cases. Experienced practitioners know that extrasystoles are at least as frequent in cases coming to a doctor's office. Therefore it becomes apparent that the treatment of the cardiac irregularities is one of the important services rendered by the physician to his clientele. Moreover, the treatment of the cardiac irregularities is today, comparatively speaking, very efficacious and easily carried out.

I shall first discuss the treatment of auricular fibrillation because this makes up nearly one half of all the cases of cardiac irregularity that one has to treat and because it has a very harmful effect on the pumping mechanism of the heart. Eyster and Swarthout<sup>2</sup> have shown that the mere presence of auricular fibrillation in a dog's heart reduces the output of the heart by an average of 40 per cent and reduces the blood pressure on an average of 35 per cent. Lewis<sup>3</sup> demonstrated that auricular fibrillation not only reduces the output of the heart but also may increase the venous pressure even in an animal with an otherwise normal heart. These experiments indicate that the appearance of auricular fibrillation in hearts with a valvular defect or with a damaged myocardium is a most serious occurrence. Every experienced physician has noted that patients with mitral stenosis often do very well for many years but that the onset of the absolutely irregular pulse, which is synonymous with auricular fibrillation, brings about cardiac failure, which from that time on is present in some degree unless the auricular fibrillation is properly treated. I have seen athletes performing creditably in competition despite the pres-

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22. Eggleton, P., and Eggleton, G. P.: Biochem. J. 21:190, 1927.

23. Millikan, G. A.: Proc. Roy. Soc. London, S.B. 120:366 (June 2) 1936; 123:2181 (July 1) 1937.

ence of a mitral stenosis. But as soon as auricular fibrillation began, symptoms of breathlessness and dropsy appeared and from that time on the former athlete was more or less of an invalid and could at the best carry out duties entailing only very moderate exercise.

In man, the effect of untreated auricular fibrillation is largely to increase the venous pressure and to decrease the output of blood leaving the ventricles during each minute. Through the influence of vaso-motor adaptation, the tendency for blood pressure to drop is usually counteracted. The reduction in ventricular output is due largely to the rapid rate of the ventricles, to the large number of premature and abortive contractions of these chambers and to auricular paralysis. Digitalis given in sufficient amounts will reduce the ventricular rate to the optimum, and in reducing the rate of the ventricles the number of premature and abortive contractions becomes very small indeed. It is therefore by partially blocking conduction from the fibrillating auricles to the ventricles that digitalis brings about its remarkably favorable influence on the heart in auricular fibrillation.

When one sees a patient with auricular fibrillation for the first time, the ventricles are usually beating with an absolutely irregular rate of from 100 to 160 beats a minute. The exhibition of sufficient amounts of digitalis will reduce the rate of the ventricles to a value of from 60 to 70 beats a minute, which in most adults I find to be the optimal rate when auricular fibrillation is present. The effect on the patient is remarkable. As a rule, as soon as the rate is reduced to the optimal value the patient's dyspnea lessens, tenderness and enlargement of the liver recede, edema begins to become absorbed and to be excreted by the kidneys, and the cyanosis tends to diminish. The increased venous pressure, which is the main factor in causing the symptoms of dyspnea, edema and swelling of the liver, drops to normal values; measurements of circulation time and of minute volume show that the output of the heart has approached the normal, even when serious valvular defects and myocardial damage are present.

It is true that digitalis increases the mechanical efficiency of the heart muscle fibers, as Visscher<sup>4</sup> has shown, but when auricular fibrillation is present the reduction in the ventricular rate is at least as great a factor in bringing about compensation in cardiac failure, if not a greater one.

#### METHOD OF GIVING DIGITALIS

There has been a great deal of discussion as to the method of giving digitalis, and I shall spend some time in discussing this, emphasizing the methods that have proved themselves of great value in the treatment of a large number of cases at the Minneapolis General Hospital and at the University outpatient heart clinic. I shall discuss mainly the use of preparations of digitalis purpurea for preparations of this drug are now carefully standardized in terms of the cat unit.<sup>5</sup> This drug

4. Visscher, M. B.: *The Energy Metabolism of the Heart in Failure*, Minnesota Med. 21:85 (Feb.) 1938.

5. A cat unit as used in this paper is the amount of drug per kilogram of body weight necessary to kill a cat in one hour under the standard conditions of the original Hatcher-Brody method. The cat unit as determined by other methods such as the Magnus differs considerably from the Hatcher-Brody cat unit. The value of the cat unit lies in the fact that the body weight of the patient, one can calculate necessary to obtain the optimal digitalis effect the level of toxic effects of the drug. Maintenance dosage can also be expressed in cat units per day. At present digitalis is standardized according to the U. S. P. XI so that 0.65 cc. of the tincture or 0.065 Gm. (1 grain) of the powdered leaf is 1 Hatcher-Brody cat unit. In the previous editions of the U. S. Pharmacopeia 1 cc. of tincture or 0.1 Gm. of the powdered leaf contained 1 cat unit. One-tenth Gm. (1½ grains) of the standard U. S. P. XI powder is equivalent to 1.6 Hatcher-Brody cat unit.

has now been so thoroughly studied that it is known approximately how much a patient should be given to get a desired effect and just about what the toxic dose for a given patient is. I shall mention briefly the use of preparations from digitalis lanata. In my opinion 1 cat unit (0.65 cc. of tincture or 0.065 Gm. [1 grain] of U. S. P. powdered leaf) to each 10 pounds (4.5 Kg.) of body weight when anchored in the body gives very nearly the optimal effect in lowering the ventricular rate in auricular fibrillation. It is also with but rare exceptions a perfectly safe amount. If this amount does not effect the desired lowering of the ventricular rate, a little more (from 10 to 30 per cent) most certainly will. On the other hand, not more than one patient in fifty will show signs of digitalis intoxication with this amount, and the degree of intoxication will not be serious. Stopping the administration of digitalis for from twenty-four to seventy-two hours will relieve the symptoms of intoxication and no harm will have been done. Moreover, the administration of 1 cat unit a day will on the average hold the ventricular rate of a patient weighing 150 pounds (68 Kg.) at rest and free from nervousness at the optimal point. In other words, the anchored digitalis is removed from the body at the rate of approximately a cat unit a day. Doses of digitalis of this size will not reduce the volume flow through the coronary arteries nor injure the myocardium. One cat unit a day may be given to the 150 pound patient for years without danger. If vomiting necessitates rectal administration, the same dose is to be given as for the oral administration.

Whether one uses tincture or whether one uses pills or capsules of the powdered leaf is in my opinion immaterial provided the tincture is fresh and is standardized accurately. As a rule equally good results will be obtained by the two forms of the drug.<sup>6</sup> If the patient is only moderately decompensated, seven days may be taken for optimal digitalization. In this case 21 cat units would be given to a patient weighing 150 pounds to be used up in seven days: 6 cat units to supply the loss of digitalis in the six days following the day on which the drug is first given and 15 cat units for the optimal amount to be anchored in the body.<sup>7</sup> It is well if the patient can be seen by the physician daily, but many of our dispensary patients are not seen until the week has passed. If the ventricular rate is above 70 when the patient returns and is resting quietly in the examining room and is not excited, we give 2 cat units a day until the heart rate is between 60 and 70 beats a minute. When this rate has been reached, we give 1 cat unit a day. It is best if the physician can see his patient every day or two to control the rate by giving a little more or a little less digitalis for the next four weeks, but many of our patients cannot return for one or two weeks, and it is rare not to find the pulse rate approximately the same. A little more or a little less digitalis will bring about the desired rate (60-70).

In our dispensary practice we often give the calculated optimal amount within a shorter period if the patient is badly decompensated. For example, we frequently give a patient weighing 150 pounds 17 cat units throughout a three day period, during which time a

6. The tincture should not be given in drops but the required amount should be measured out in a measuring glass. I prefer to mix 0.6 cc. of tincture of digitalis with 3.4 cc. of aromatic elixir and give this fairly pleasant mixture in this dose, each drachm (4 cc.) representing 1 cat unit.

7. Assuming that the patient has had no digitalis for at least three weeks. If the patient has had digitalis recently, 2 cat units a day is given until the pulse rate reaches 60-70.



visiting nurse counts the ventricular rate with the stethoscope during daily visits to the patient's home or to a rest home in the city if the patient is from out of town. The nurse reports late each afternoon to the physician in charge of the case.

When the patient returns on the third day, the dispensary physician gives 1 or 2 cat units a day for the next three days, depending on whether the ventricular rate is in the neighborhood of 60-70 or higher. Given in this way we have seen digitalis poisoning occur only infrequently, and we have yet to see the first case of dangerous intoxication. On the other hand, the results on the ventricular rate have nearly always been excellent.

In our hospital practice we usually attempt to get the optimal result more quickly. As a rule we give 15 cat units to the 150 pound patient within the first thirty-two hours, one third of the calculated amount being given at once and one sixth every eight hours for four doses. An attempt is made to hold the ventricular rate at the optimal point by the exhibition of 1 cat unit a day if the optimal rate has been reached at the end of from forty to forty-eight hours. If this rate has not been reached we give 2 cat units a day until the rate is between 60 and 70. After this 1 cat unit a day will usually hold the rate at this point. It may be necessary to give a little more or a little less, but if the patient is seen each day the desired amount can readily be found by observation of the pulse rate with the patient at rest and in a nonexcited state.

Occasionally we have a desperate case of heart failure with auricular fibrillation with a high ventricular rate (150-200) in which it appears desirable to reduce the rate even more rapidly. In such a case we resort to intravenous medication. In my opinion digitalis lanata preparations are best for this purpose, though one can dilute an ordinary tincture with saline solution and inject intravenously or use ampules of a well known preparation such as digalen or digifolin. Eight cat units of digitalis purpurea can be given safely at one injection to a patient weighing 150 pounds. I prefer to give 1 mg. of digitanid C\* or 1 mg. of digoxin to such a patient. Both of these are preparations of digitalis lanata. The report of the following case will illustrate how efficiently these preparations can work:

A woman aged 56, with high blood pressure and electrocardiographic evidence of coronary arteriosclerosis, suddenly had dyspnea and orthopnea with auricular fibrillation. After sticking it out for one week at home she entered the hospital, showing 3+ edema of the lower extremities and some puffiness about the eyes. Cyanosis, ascites and venous distention of the vessels of the neck were present. The apical rate was 145 and totally arrhythmic. The venous pressure at the level of the right auricle was 17 cm. of water. There were rales at both bases as high as the angle of the scapula. The liver was down 6 cm. The vital capacity was 900 cc. She was given 1.6 mg. of digitanid C shortly after the examination on admission. Two hours later the apical rate was 84, the venous pressure 8 cm. of water and the vital capacity 1,600 cc. She was given digitanid C orally, 0.8 mg. a day, under which her pulse ranged between 60 and 80 during the following week. Twenty hours after admission all rales had disappeared, cyanosis had disappeared and the dyspnea had lessened remarkably. On the second day in the hospital the fluid intake was 600 cc. and the output 2,200 cc. During the first week in the hospital the fluid output exceeded the intake by 6,200 cc. and all visible edema

had disappeared. On the fourth day the liver was back at the costal margin; on the third day the vital capacity was 2,400 cc., which was about her normal value. On the tenth day the patient was allowed up and around and showed no signs of dyspnea, nor had she any distress. No other treatment other than rest and digitalis was used.

This case illustrates not only how digitalis properly given can favorably affect auricular fibrillation complicating cardiac failure but how rapidly a digitalis preparation can accomplish the result when intravenously administered.

It cannot be denied that there are a few exceptions to the foregoing rules for administration of digitalis; occasionally digitalis seems to have no appreciable effect on conduction of the impulse from the auricles to the ventricles and therefore does not slow the ventricular rate, and a small percentage of patients show toxic symptoms before the optimal results in reducing ventricular rate can be accomplished. Not a few patients will need more than 1 cat unit to 10 pounds of body weight anchored in the body in order to produce optimal slowing of the pulse rate. Usually not more than from a 10 to 30 per cent increase is necessary to accomplish this. A very few patients will need less than the calculated optimal dose. This condition is usually found in coronary disease or in other conditions that in themselves reduce conductivity through the bundle of His. These cases often show apical rates of 100 or less before any digitalis has been given. When the apical rate is less than 110 it is well to use smaller amounts of digitalis than that previously recommended because conductivity from auricles to ventricles may already be impaired. If the rate is around 80 only 2 cat units a day should be given and the pulse should be watched from day to day until the physician is certain that the rate is not going to fall below 60. In hyperthyroidism digitalis usually fails to lower ventricular rate and its value is questionable. The administration of compound solution of iodine will usually reduce the rate somewhat. Operation should be carried out when it is thought safe, and after operation the fibrillation will disappear in more than 50 per cent of the cases. In toxic conditions associated with fever the dosage should be definitely smaller." The effect will often leave much to be desired, but according to the present state of our knowledge it seems unwise to go beyond one-half the usual dose in fevers with toxemia.

There are patients who are sensitive to digitalis and the reduction of their ventricular rate may be difficult. It is necessary to proceed with smaller doses, and it may be impossible to get the rate below 80-90. When more digitalis is given nausea, vomiting or extrasystoles may appear, and the patient who was beginning to compensate moderately may now show signs of decreasing compensation. One should give as much digitalis as the patient can stand without showing signs of nausea, vomiting or extrasystoles. Coupled beats developing during the course of digitalis treatment mean severe digitalis intoxication, and the drug must be withheld until all extrasystoles disappear. It may then be cautiously given again.

The ventricular rate should never be allowed to drop below 60. Lowering the pulse rate below 60 does not increase but rather decreases the efficiency of the cardiac

8. This is a preparation of digitalis lanata studied by Dr. M. R. Vissecher pharmacologically and now being investigated clinically in the Minneapolis General Hospital. The drug, prepared by the Sandoz Company, has not yet been released to the profession.

9. Edmunds, C. W.; Smith, R. G., and Moyer, C. A.: The Sensitivity of the Diphtheritic Heart to Digitalis, *J. Pharmacol. & Exper. Therap.* 61:286 (Nov.) 1937. Hirschfelder, A.; Bieck, J.; Kucera, F. J.: The Effect of High Temperature on the Action and Toxicity of Digitalis, *ibid.* 15:427 (July) 1920.

pump. Signs of decompensation usually do not reappear until the rate falls to 50 or below, but 60 should be the lower limit of the pulse rate at rest.

#### QUINIDINE

Up to this point I have been discussing the treatment of auricular fibrillation in patients who had in addition a valvular disease or a diseased myocardium. There are a few patients who have attacks of auricular fibrillation unassociated with any discoverable organic heart disease. These attacks may be associated with great excitement or emotion. For example I have seen one patient who had a number of attacks of auricular fibrillation following the excitement of the sexual act. Occasionally severe physical exertion will bring on an attack. I have observed one such case in a track athlete. Attacks of auricular fibrillation may follow infectious diseases such as influenza and pneumonia. Drugs and chemicals may induce attacks. In my experience attacks of auricular fibrillation following drinking bouts are not at all uncommon. The outlook in these cases is excellent as a rule and the patient usually suffers only from palpitation, smothering, weakness, mild precordial distress or a little dizziness. Occasionally cardiac failure will develop even though there is no evidence of the presence of organic heart disease. As a rule the fibrillation is easily terminated in these cases and normal rhythm restored by the use of quinidine. As far as my reading goes all who write on this subject agree that quinidine is the drug of choice in auricular fibrillation unaccompanied by serious organic heart disease.

On the other hand there are many competent cardiologists who warn against the use of quinidine to terminate auricular fibrillation in cases of organic heart disease or who overemphasize the dangers of quinidine in the treatment of auricular fibrillation complicated by organic disease of the heart. We have used quinidine to terminate auricular fibrillation for the past seventeen years and during this period my associates and I at the Minneapolis General Hospital and at the University Heart Clinic have treated with quinidine more than 500 patients having auricular fibrillation. In approximately 65 per cent of these cases the auricular fibrillation has been stopped and the ventricular rhythm has become regular. Moreover we have prevented the return of fibrillation in nearly every patient who has continued the daily dose prescribed for prophylaxis. In general we are well satisfied with the results of quinidine therapy in our cases. Many patients who were uncomfortable and unable to carry out even moderate physical exertion on digitalis therapy alone were made easy and recovered considerable ability to carry on physical exertion after quinidine had restored normal rhythm.

That there are grave dangers inherent in the use of quinidine I do not deny. Quinidine is a drug which is toxic for the heart muscle. It reduces the strength of contraction of the heart muscle and in our early use of the drug we occasionally brought on cardiac failure while attempting to terminate auricular fibrillation.<sup>10</sup> Since then we have learned that the use of quinidine in treating auricular fibrillation in hearts that have been decompensated or that present serious organic disease must be preceded by thorough digitalization of the heart. Under these circumstances cardiac failure will not develop even when large doses of quinidine are

given. Before giving quinidine we give sufficient digitalis to bring the ventricular rate to values around 60-70. This rate is maintained by daily doses for approximately two weeks before quinidine therapy is started. If the patient was severely decompensated before digitalis therapy was started we might wait a little longer before beginning the quinidine therapy. Under these circumstances we do not fear the adverse effect of quinidine on the mechanical efficiency of the heart muscle.

Another danger that is only rarely encountered when quinidine is used is that of asystole. I myself have observed only one case:

A woman aged 36 who had rheumatic fever in her youth was seen by a local physician in an advanced stage of cardiac failure associated with mitral stenosis and auricular fibrillation and a greatly dilated heart. She was overdigitalized and during the period that her heart was showing coupled beats she was given quinidine. When 30 grains (2 Gm.) was given unconsciousness developed. Her physician observed five attacks of asystole in three hours and called me in consultation. She recovered and her heart was kept regular for three years. Auricular fibrillation reappeared and in a few months she died of multiple embolism.

It should be noted that these emboli did not develop during the period when quinidine restored and maintained regular rhythm but at a time when the auricles were fibrillating. In reviewing this case critically I would say that two mistakes were probably made. Quinidine should not be given in doses larger than 15 grains (1 Gm.) a day when there is evidence of digitalis poisoning because there may result therefrom a dangerous summation of the toxic effects of both drugs. This patient was suffering from digitalis intoxication (coupled beats) when the quinidine was administered. It would have been better to wait one week after all signs of toxicity had disappeared before starting quinidine. Moreover, this patient had a markedly dilated heart as shown by x-ray and postmortem examination. In such cases it is advisable either to withhold quinidine or to proceed more slowly in increasing the dose.

Embolism is a danger that undoubtedly is associated with the use of quinidine but one that has been overemphasized in my opinion. The paralyzed auricle is a favorite site of mural thrombi. When the auricles beat again a piece of thrombus may be dislodged and become an embolus. In my experience embolism is less frequent following the restoration of regular rhythm with quinidine than it is in cases in which only digitalis is used and in which the auricles are allowed to fibrillate. Viko, Marvin and White<sup>11</sup> have shown that embolism occurred in 4.5 per cent of their untreated cases and in 3.1 per cent of their cases treated with quinidine. Korns<sup>12</sup> questions the greater incidence of embolism in quinidine-treated cases. Parkinson and Campbell,<sup>13</sup> after a careful analysis of embolism in quinidine therapy, came to the conclusion that this danger has been overemphasized. I have not infrequently seen embolism follow resumption of fibrillation in auricles that had been kept regular for long periods on quinidine.

Cases of syncope occur rarely. I myself know of only one such case. The patient was treating himself and it was proved that he had been taking excessive doses at times. Epileptiform convulsions are also rare

11. Viko, L. E.; Marvin, H. M., and White, P. D.: A Clinical Report on Quinidine Sulfate, *Arch. Int. Med.* **31**: 345 (March) 1923.

12. Korns, H. M.: An Experimental and Clinical Study of Quinidine, *Arch. Int. Med.* **31**: 36 (Jan.) 1923.

13. Parkinson, J., and Campbell, M.: Quinidine Treatment of Auricular Fibrillation, *Quart. J. Med.* **22**: 281 (Jan.) 1929.

10. Eyster, J. A. E., and Fahr, George: Observations on the Use of Quinidine in Auricular Fibrillation, *Arch. Int. Med.* **29**: 59 (Jan.) 1922.

episodes in patients who are abnormally sensitive to quinidine. I have observed one such case in the University Hospital. Convulsions followed a dose of only 6 grains (0.4 Gm.). The most common manifestations of sensitivity to quinidine are epigastric distress, nausea, vomiting, headache, diarrhea, ringing in the ears, palpitation and apprehension. These symptoms should lead to a lowering of the dosage and to a less rapid increase in dosage up to the point at which auricular fibrillation is stopped. Very frequently one will be successful with a less rapid increase in dosage. If these symptoms do not disappear and if they become annoying it is best to stop the quinidine altogether.

Having first stated the disadvantages of quinidine, I shall now give an account of its value in treatment. There is no question in any one's mind that quinidine is the treatment *par excellence* in auricular fibrillation not associated with serious organic heart disease and when auricular fibrillation in hyperthyroidism is still present two weeks after thyroidectomy. As a rule these cases show regular heart rate on small doses of quinidine and unpleasant episodes are very rare. Kerkhof<sup>14</sup> and others have shown that the efficiency of the heart is increased 25 per cent in mitral stenosis with auricular fibrillation when regular beating of the auricles is restored even though the heart was kept at an optimal rate by the use of digitalis during the period of fibrillation. I therefore recommend a trial of quinidine in all cases of mitral stenosis with auricular fibrillation in which the total transverse diameter of the heart is not enlarged more than 20 per cent and when the abnormal rhythm has not been present for more than six months. The physician who is experienced in the use of quinidine may extend these limits, but the beginner should stay within them. The use of quinidine must be preceded by digitalization and the heart must have been well compensated for two weeks before the quinidine therapy has been started. Digitalis must be given through the treatment with quinidine; we often continue it after the cardiac rate has become regular in cases of marked cardiac enlargement. Quinidine must be given every day after the rhythm has become regular because most hearts will revert to the absolutely irregular rate from weeks to months after the drug has been discontinued. Patients must be warned not to discontinue the drug. The average case will continue with regular rhythm on 9 grains (0.6 Gm.) a day. Occasionally we give 12 grains (0.8 Gm.) a day. Rarely we give 1 Gm. or 15 grains, a day to keep a heart regular. I have given doses of 9 and even 12 grains a day for as long as ten years and have never yet had occasion to regret it. I believe that continuance of regular rhythm in mitral stenosis will increase life expectancy materially.

Physiologists agree that the auricles contribute to the filling of the ventricles. Wiggers<sup>15</sup> states that they contribute on an average 35 per cent of the total filling, which would indicate that the auricle is an important part of the pump mechanism. If the auricles do not contract, venous pressure must rise or the cardiac output will fall even in a normal heart. Rise in venous pressure is the fundamental mechanism in bringing out the symptoms of dyspnea and edema. For this reason, and also because many patients feel much better

when the heart rate is regular, we try quinidine therapy in cases of auricular fibrillation associated with hypertensive heart disease and coronary arteriosclerosis. In these older patients quinidine seems to have no more contraindications than in the younger ones with mitral stenosis. The same rules for administration apply in these cases.

We administer quinidine in 3 grain (0.2 Gm.) tablets. One tablet is given on the first day to test the patient for intolerance to the drug. The next morning one tablet is given at 8 o'clock and another at 9. On the third day one tablet is given at 8, one at 9 and one at 10 a. m. The dosage is increased one tablet a day, all the tablets being given at 8, 9 and 10 a. m. It might even be safer to use 2 grain (0.13 Gm.) tablets and proceed in the same way but more slowly. We prescribe as high as twelve tablets, or 36 grains (2.3 Gm.), a day but I would recommend that the inexperienced physician stop at a daily dose of 24 grains (1.5 Gm.). With this dose at least 50 per cent of all cases should have regular rhythm restored. The physician should prescribe 9 grains (0.6 Gm.) a day for the purpose of maintaining the regular rhythm as long as possible. If a patient weighing 150 pounds was severely decompensated before starting the digitalis I recommend continuing with 1 cat unit a day in addition to the 9 grains of quinidine. During the treatment the patient should be in a hospital or at home with a nurse to observe the pulse and general condition until the pulse becomes regular. Many of our patients are treated at home. A visiting nurse sees the patient once a day and reports to me each evening until the pulse is regular.

The incidence of auricular flutter is much less than that of fibrillation. In this condition the auricle is beating at a rate of from 260 to 320 a minute, but as a rule there is a 2:1 heart block. In my experience auricular flutter is frequently found in hearts that present only a moderate degree of organic disease, and the patients when seen by the physician are not suffering from the severest degrees of cardiac failure despite the fact that the ventricular rate is between 130 and 160 beats a minute. Occasionally one sees a case of auricular flutter in which there is no heart block; then the ventricle is beating at a rate of 260 or over. This is a most dangerous rate and even in an otherwise normal heart cannot go on unchecked if the patient is to live. The rate of the ventricle must be reduced at once, and with very rare exceptions this can be easily brought about by the exhibition of digitalis. In the case of the very high ventricular rates in which no block is present I recommend strongly the intravenous use of a preparation of digitalis, preferably a lanata preparation, because of the rapidity with which they work when given intravenously. When a 2:1 heart block is present and the patient is not suffering critically, digitalis may be given orally or rectally in such doses that the optimal amount of 1 cat unit to 10 pounds of body weight is introduced into the body within a period of from twenty-four to thirty hours. This will usually increase the block to a 3:1 or 4:1 block. I prefer to give enough digitalis to keep the block 4:1. Very frequently the previously regular beat of the 2:1 block will become somewhat irregular after the exhibition of large doses of digitalis because the heart will slip from 4:1 block back to 3:1 block and then again into 4:1 block. A good rule is to keep the rate of the ventricle between 60 and 70 beats a minute. A main-

14. Kerkhof, A. C.: Minute Volume Determinations in Mitral Stenosis, *Am. Heart J.* 11: 206 (Feb.) 1936.  
15. Wiggers, C. J.: *Modern Aspects of Circulation in Health and Disease*, ed. 2, Philadelphia, Lea & Febiger, 1923, p. 96.

tenance dose of 1 cat unit or more a day should be given to the patient in order to hold this rate.

In about 90 per cent of cases the auricular flutter will change to auricular fibrillation if this state of digitalization is kept up for a week or two. Digitalis is then stopped and in about 60 per cent of the cases that have gone over to fibrillation normal rhythm returns. I have found it advisable to give quinidine in those cases in which fibrillation does not develop after digitalization and in those in which fibrillation is not followed by normal rhythm after digitalis has been removed. We give quinidine to patients with flutter according to the same rules outlined for giving quinidine to a patient with auricular fibrillation. The percentage of success in bringing about return of a normal cardiac mechanism with quinidine is no greater in flutter than in fibrillation. A certain number of patients will remain refractory, and it is necessary to continue these patients on digitalis therapy in order to block conduction from auricles to ventricles. Starr<sup>16</sup> states that acetyl- $\beta$ -methylcholine will occasionally convert auricular flutter to regular mechanism if from 30 to 50 mg. is given subcutaneously. This drug, the action of which will be discussed under paroxysmal tachycardia, can be tried for flutter when other methods fail.

#### EXTRASYSTOLES

Extrasystoles or premature beats are seen in the doctor's office as frequently as auricular fibrillation. Most of these cases do not present serious organic heart disease, and unless the extrasystoles occur more frequently than 12 a minute they do not affect the efficiency of the heart adversely. Extrasystoles not associated with organic heart disease are usually found in nervous, worried or apprehensive persons. I have occasionally seen an athlete retired from the squad for this irregularity. On reassurance and treatment he has soon gone back to successful competition. Frequently extrasystoles are associated with flatulence, the relief of which causes the premature beats to disappear. The patient usually does not suffer from symptoms of cardiac failure but is embarrassed and frightened by what he terms his heart "flopping" or "skipping a beat" or "stopping" for an instant or "palpitation" or a "funny feeling in the heart." Treatment in these cases requires first of all reassurance that the condition is not serious. Worry and undue fatigue must be removed. A change of environment is often useful. Sedatives such as bromides, barbiturates or codeine may be necessary to reduce excitability. Occasionally tobacco or coffee must be prohibited. Sometimes lying on the left side will evacuate gas from the stomach and get rid of extrasystoles. When these measures fail, quinidine either alone or with strychnine one-thirtieth grain (0.002 Gm.) three times a day will frequently abolish this irregularity. The quinidine is to be given in doses of 3 grains three times a day increasing to four times a day or even to 4 grains three times a day.

Extrasystoles are found in at least 10 per cent of all cases of coronary thrombosis. Masters<sup>17</sup> found them in 25 per cent of the Mount Sinai Hospital cases. Here they are of grave significance and quinidine must be given to prevent the appearance of ventricular tachy-

cardia, the drug being given in doses of 3 grains every two to three hours for three or four doses. If the extrasystoles disappear the drug may be repeated every six to eight hours to prevent recurrence. Digitalis predisposes to the formation of extrasystoles and ventricular tachycardia in coronary thrombosis and should not be administered unless auricular fibrillation or flutter with ventricular rate above 95 or moderately severe cardiac failure is present. When extrasystoles occur in the course of valvular disease, in the course of hypertension or in the course of coronary arteriosclerosis they may be of serious significance, especially if they occur at frequent intervals. Quinidine or quinidine and strychnine should be used to stop them, given as already outlined. As a rule, digitalis should not be given under these circumstances.

#### PAROXYSMAL TACHYCARDIA

Paroxysmal tachycardia is, after all, only a very rapid and regular series of extrasystoles, starting suddenly and ending just as suddenly. I shall first discuss the treatment of paroxysmal tachycardia of auricular and junctional origin. In some cases these attacks come on infrequently and last only a short time, and in these there is no need for treatment. If the attacks come on at frequent intervals and embarrass the patient, digitalis in my experience will often prevent them. I would recommend giving as much digitalis as was recommended for treating auricular fibrillation, attempting to get the optimal amount into the body within three days and holding on 1 cat unit a day from then on. I have had more success in preventing auricular and junctional paroxysmal tachycardia with digitalis than with quinidine. On the other hand, some cardiologists use quinidine for this purpose. In my hands it has been effective only occasionally.

An attack of paroxysmal tachycardia usually leads to much discomfort and may have serious consequences in a patient who has serious cardiac disease. It is therefore necessary to know how to treat the attack. The patient is usually recumbent when the physician arrives. An ice bag over the precordium helps psychically. I would first try pressing on the carotid sinus, as this occasionally stops an attack. One places the second and third fingers over the carotid artery at the level of the thyroid cartilage and presses the artery very firmly back against the transverse processes of the cervical vertebrae. It should be tried first on the right carotid and then on the left. If this doesn't stop the attack I try pressing on the eyeballs. Sometimes the patient can stop an attack by closing the glottis after a deep inspiration and then pressing hard. A feather, tongue depressor or other object pressed or rubbed against the posterior pharynx so as to cause vomiting will also occasionally stop an attack. Weiss and Sprague<sup>18</sup> recommend giving from 1 to 2 drachms (3.8 to 7.5 cc.) of fresh syrup of ipecac to cause nausea and vomiting. If the effect is not obtained after forty-five minutes the dose is repeated or increased a little. This method is very efficacious. Acetyl- $\beta$ -methylcholine has recently been recommended<sup>16</sup> for the treatment of paroxysmal tachycardia of auricular or junctional origin. It is probably the surest in its action of all the drugs recommended for treating attacks. There seems to be no great danger connected with its use. I have seen one case in which there was

16. Starr, Isaac, Jr.: Further Studies on Paroxysmal Tachycardia, *Am. J. M. Sc.* 191: 210 (Feb.) 1936.

17. Masters, A. M.; Dack, S., and Jaffe, H. L.: Disturbances of Rate and Rhythm in Acute Coronary Artery Thrombosis, *Ann. Int. Med.* 11: 735 (Nov.) 1937.

18. Weiss, Soma, and Sprague, H. B.: Vagal Reflex Irritability and the Treatment of Paroxysmal Tachycardia with Ipecac, *Am. J. M. Sc.* 194: 53 (July) 1937.

a short period of unconsciousness following a dose which was about double the amount I recommend in this paper. The drug is a powerful stimulator of the vagus and should not be used when there is a tendency to asthma, as its injection will bring on an attack. It produces sweating, vomiting and vasodilatation and occasionally substernal pain and defecation. I would recommend trying 20 mg. of the drug in younger patients and 30 in older patients. The drug is obtained from Merck & Co. in powder form and must be dissolved in water and prepared for hypodermic use. It is very soluble and 50 mg. can be given in 1 cc. The drug is given subcutaneously and the deposit is massaged to increase the effect if necessary. I have not yet needed to supplement the drug effect with carotid sinus pressure, though Starr claims that 20 per cent of his patients needed it. The patient should be lying down, since he may faint if he is sitting up. If the attack does not stop in two or three minutes the dose is repeated. Correspondingly smaller doses should be used in children or very small adults. Large intravenous doses of digitalis will also stop attacks. Ten cc. of digifolin or digalen in ampules may be given to the patient weighing 150 pounds in one or two doses.

Paroxysmal tachycardia of ventricular origin, or ventricular tachycardia as it is usually designated, is not infrequently discovered in patients who seem to have no organic heart disease or cardiac enlargement. Because of the rapid rate (160-220) one often finds signs of failure even when there is no evidence of any other cardiac disease. I have a number of patients who come in at long intervals with attacks and moderately severe cardiac failure. When the tachycardia is stopped they return to a life of moderately strenuous activity. There are no signs of any cardiac failure as long as they take 9 grains (0.6 Gm.) of quinidine a day. They then become convinced that they will never have another attack, omit the drug and sooner or later return with tachycardia and symptoms. In one case which I saw in consultation with Dr. Scherer, it was necessary to give 85 grains (5.5 Gm.) in five hours in order to stop the tachycardia and relieve the alarming symptoms of cardiac failure which had developed in an otherwise normal heart. This patient was like many whom I have seen in that she had been having attacks for years, the attacks becoming progressively more severe, lasting longer and being associated with alarming symptoms of cardiac failure soon after she went off her daily prophylactic dose of 9 grains.

As a rule this type of tachycardia is found most frequently in patients with coronary disease and may then be a most serious factor. It is not at all infrequent in coronary thrombosis and in that case is the next step before ventricular fibrillation and death. The need for an efficacious drug is imperative and it is fortunate that quinidine is available. I have never failed to stop ventricular tachycardia with quinidine. In ventricular tachycardia it is well to give 3 grains of quinidine to test out the patient for idiosyncrasy to the drug and then give 6 grains an hour later. If the tachycardia has not stopped by the end of the hour, 6 grains may again be given. Even though the tachycardia may not have ceased at this time I would stop giving the drug and wait four hours before repeating it. It has been shown by Lewis<sup>19</sup> that the maximal effect on ventricular rate comes four hours after quini-

dine is given by mouth and most attacks of ventricular tachycardia will stop with a total of 15 grains (1 Gm.) given in this way. There is usually time enough to save the patient's life after the four hours has elapsed. I have had success with smaller doses and I have also had patients who needed much more. There is one question that will arise in the minds of readers of this paper, namely as to the use of digitalis in these cases. Digitalis increases the tendency to ventricular tachycardia in coronary thrombosis and, once the tachycardia is established, it probably increases the tendency to ventricular fibrillation. Therefore digitalis should not be given when ventricular tachycardia is present.

#### HEART BLOCK

The treatment of heart block in my experience is the least satisfactory treatment of any of the arrhythmias. Occasionally atropine in doses of  $\frac{1}{100}$  grain (0.0006 Gm.) will so far reduce the block in the bundle of His in cases of partial heart block that digitalis may be used safely in moderate dosage to increase the mechanical efficiency of the heart muscle. In total heart block digitalis may be given to increase the mechanical efficiency of the heart muscle without fear of any reduction in ventricular rate. When attacks of asystole with syncope are occurring, from 5 to 10 minims (0.32 to 0.65 cc.) of epinephrine subcutaneously given with massage of the area will prevent asystole and syncope for from one to two hours. At the time of asystole there is no blood flow, and if the asystole with syncope and convulsions lasts from thirty to sixty seconds epinephrine from 3 to 5 minims (0.2 to 0.3 cc.) must be given intracardially in the fourth left interspace just lateral to the sternal border. Ephedrine hydrochloride in capsules containing three-fourths grain (0.048 Gm.) may be given from four to six times a day to patients having daily attacks of Adams-Stokes syndrome due to asystole of the ventricles. These patients in my experience seem very tolerant to ephedrine and can be given large doses without very unpleasant side effects. I have apparently inhibited the Stokes-Adams syndrome for long periods by chronic doses of ephedrine, although it must be admitted that it fails in some cases to prevent attacks. Wherever possible an electrocardiogram should be taken because the Adams-Stokes syndrome may be due to runs of ventricular fibrillation or of frustrate extrasystoles. In this case neither epinephrine nor ephedrine should be given, for it only increases this tendency, but rather quinidine in sufficient doses to stop the runs of ventricular fibrillation or to inhibit the frustrate extrasystoles.

#### ABSTRACT OF DISCUSSION

DR. WILLIAM J. KERR, San Francisco: In the main, I agree with what Dr. Fahr has said about the treatment of disturbances in the mechanisms controlling the heart. I agree with what he said about digitalis, with one possible exception. I believe there are patients who have advanced mitral stenosis with a button-hole mitral valve who will not do well if the ventricular rate is reduced to the level which he suggests. Some of these patients, I am sure, will be better off at a rate of from 80 to 90 than at the lower figure. Dr. Fahr wisely suggests that there is no need for the extremely rapid digitalization of patients which was suggested a few years ago. If the result can be achieved in three or four days in the average person, that is the most satisfactory method. I agree with Dr. Fahr that the dangers of quinidine have been overrated, excepting in older persons who already have some degree of heart block, to whom

19. Lewis, Thomas: Value of Quinidine in Cases of Auricular Fibrillation, *Am. J. M. Sc.* 163:781 (June) 1922.

I think it should be given with great caution. I believe it is far better to give the quinidine regularly about every five or six hours around the clock in preference to single doses given early in the morning. I think that if cases are chosen properly and it is given regularly throughout the day and night the results will be much higher than 50 per cent and will approach 80 per cent in practice. Dr. Fahr did not have a chance to speak of extrasystoles, paroxysmal tachycardia, ventricular tachycardia and heart block. I should like to make one point about ventricular tachycardia which I hope he will discuss in closing. It is suggested that quinidine should be used more frequently in ventricular tachycardia. If all patients with ventricular tachycardia are given quinidine there will be real trouble because a high percentage of these patients have serious vascular disease of the heart. A good many of them have block in the conduction system and since quinidine acts on the conduction system tending to increase the block as well as on the muscle, I think the dangers of making the patient worse and producing a ventricular fibrillation are considerable in this group. While there are some reports of good results in this abnormal mechanism, I believe it is a dangerous drug to use in a routine manner under these circumstances.

DR. HORACE M. KORN, Iowa City: I wish to supplement Dr. Fahr's excellent presentation with a few remarks on the treatment of supraventricular paroxysmal tachycardia. The number of attacks may be greatly reduced by the continuous administration of quinidine sulfate in doses of from 3 to 18 grains (0.2 to 1.16 Gm.) a day. Individual attacks can be terminated by pressure over one or both carotid sinuses, pressure on the eyeballs, swallowing ice water, performing Valsalva's experiment or inducing vomiting by means of ipecac or tickling the pharynx. Attacks which are resistant to these measures may be terminated by acetyl-beta-methylcholine (mecholy). The dose is proportional to age and body weight. From 10 to 20 mg. may suffice for patients between 10 and 20 years of age, and from 40 to 50 mg. may be required for those over 50 years of age. Sixty mg. might be needed for an obese person. The average dose is 30 mg. The drug is given subcutaneously or intramuscularly, never intravenously. If the attack does not stop promptly, pressure is applied first to one, then to the other, carotid sinus. The injection may be repeated and the dose increased within ten minutes, so that if necessary as much as 100 mg. may be given in less than an hour. If the dose is too large the heart may stop beating for as long as from thirty to forty-five seconds. Before giving mecholy it is advisable to have ready a syringe containing one-fiftieth grain (0.0013 Gm.) of atropine, which is an instantaneously effective antidote, but beating will probably be resumed whether atropine is given or not, for it is impossible to keep the mammalian heart inhibited by vagus stimulation. If atropine is used it should be given intravenously. Quinidine is antagonistic to mecholy, and if the patient has taken any quinidine within twenty-four hours of the time when mecholy is given the latter may fail even if the dose employed is larger than it would ordinarily be. It has been the experience of most observers that mecholy will stop paroxysmal supraventricular tachycardia in from 80 to 90 per cent of the cases, especially when it is used in conjunction with carotid sinus pressure. The danger is practically negligible, provided cases of asthma, angina pectoris and far advanced myocardial disease are excluded. The introduction of mecholy means that at last a brilliantly successful remedy has been found for what is often an extremely intractable and serious disorder of the heart beat.

DR. S. A. WEISMAN, Minneapolis: I might add a few words about the treatment of auricular fibrillations with quinidine. As Dr. Fahr stated, it is important first to digitalize the patient and get the heart rate down to between 80 and 70. It is perhaps wise to cut down the digitalis to a maintenance dose before the quinidine is begun. I prefer to use a smaller beginning dose than Dr. Fahr does, because I believe that with this smaller dose the patient is more apt to establish a tolerance for the drug and not experience the toxic symptoms one so often reads about. I begin usually with 0.1 Gm. the first day, 0.2 Gm. the second, 0.3 Gm. the third and 0.4 Gm. the fourth day, given in doses of 0.1 Gm. each, one hour apart. Then begin, say, the fifth or sixth day with 0.2 Gm. every hour for three doses. The next day give 0.2 Gm. for four doses, making a total of

0.8 Gm. daily. From this point I usually give 5 grains (0.3 Gm.) every hour for three doses, then in a few days give 5 grains every hour for four doses, then after a few more days 5 grains in the first dose, then 10 grains (0.65 Gm.) in the second and 10 grains in the third. The final dose I use is 10 grains every hour for three doses. I usually quit at about 30 grains (2 Gm.) a day if the heart has not returned to normal rhythm, to which some 70 per cent have usually returned by that time. After the normal rhythm is once established, I begin to cut down the doses by 5 grains every two or three days until a maintenance dose is established. Then I continue giving, say, 10 grains or, in some cases, 5 grains, a day for years but always keep the patient on a maintenance dose of digitalis together with a maintenance dose of quinidine. The mitral stenosis group seems to be the most difficult to restore to regular rhythm. These cases are the most difficult to maintain regularity and are also the ones that are most apt to return to arrhythmia. The hypertension and coronary sclerosis groups react much more favorably to this treatment.

DR. WILLIAM DRESSLER, Berkeley Calif.: I should like to mention a remedy which I have used in Vienna, Austria for paroxysmal tachycardia. It is magnesium sulfate, which I use intravenously in doses of 15 cc. in 20 per cent solution, and I have had in many cases an excellent result. The effect appears in about five minutes, sometimes a little sooner. The injection is performed rather quickly, particularly in ventricular paroxysmal tachycardia after coronary occlusion. It has proved very successful, in some cases really life saving. I have never seen any unfavorable effect.

DR. GEORGE E. FAHR, Minneapolis: Those who have discussed my paper have helped greatly in attempting to cover the treatment of cardiac irregularities in fifteen minutes. Dr. Kerr has stated that when he has one of those narrow buttonhole mitral stenoses it is better to hold the rate around 80-90 rather than around 60-70. I agree if he means patients with markedly dilated heart who have been decompensated for a long time and who show ventricular extrasystoles or coupled beats when the slowing of the heart gets down below 80-90 beats per second. Signs of digitalis intoxication are always indications for less digitalis. I am surprised that Dr. Kerr can get normal rhythm with the use of quinidine in 80 per cent of his fibrillators. I have never been able to get more than 65 per cent. In cases of arteriosclerotic heart disease I am able to get a percentage up around 80 but in mitral stenosis I have great difficulty in getting more than 65 per cent to become regular. It is possible that Dr. Kerr's method of administering quinidine is better than mine. I shall try it. I am surprised about what Dr. Kerr said as to the use of quinidine in ventricular tachycardia. I have always used it in treating cases of ventricular tachycardia. In my opinion it is especially indicated when ventricular tachycardia follows a coronary thrombosis. Ventricular tachycardia is the next step on the way to ventricular fibrillation. I believe it is necessary to give quinidine to stop the ventricular tachycardia and prevent ventricular fibrillation. I have given as high as 85 grains (5.5 Gm.) of quinidine in a twenty-four hour period because I believe it is absolutely necessary to stop the tachycardia. I am grateful to Dr. Korn for discussing the use of acetyl-beta-methyl choline, or mecholy, in the treatment of paroxysmal tachycardia of supraventricular origin. As far as my experience goes I have been 100 per cent successful in stopping paroxysmal tachycardia of supraventricular origin with this drug. I believe Dr. Weisman's method of starting off with smaller doses and increasing the amount of quinidine more slowly is probably safer than my own. Dr. Weisman carries out the treatment of auricular fibrillation by his method in the ambulatory cases in his private practice in Minneapolis. He has told me that he has never had to regret the use of quinidine in that practice. I would disagree with one thing in his method: when he gets up to a fairly large daily dose, he then proceeds as fast as I do. That would be the point at which I would go more slowly. Dr. Dressler has suggested a new remedial agent for the treatment of paroxysmal ventricular tachycardia and I shall be delighted to try it out. No one need fear the use of intravenous magnesium sulfate if there is a hypodermic of calcium chloride handy on the tray in case there is trouble with the respiratory center.



## PATHOLOGY OF THE PLACENTA

WITH SPECIAL REFERENCE TO INFARCTS AND THEIR  
RELATION TO TOXEMIA OF PREGNANCY

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The pathology of the placenta may be better understood and appreciated if approached from the standpoint of the life cycle of this organ and the influences to which it is subjected from the time of implantation to full term. Accordingly, certain fundamental basic facts will be considered and the pathologic changes which may arise from each of these will be discussed.

Since this article deals particularly with placental infarction, no attempt will be made to consider in more than a brief way the various other pathologic conditions, which are fully discussed in the textbooks and literature.

Embryologically, the anlage of the placenta is trophoblastic tissue, one of the primary germ layers. As such it is endowed with peculiar invasive qualities by virtue of its proteolytic enzymes, whereby it is able to attach itself to the uterine decidua, embed in it, open maternal blood vessels and create for itself a vascular bed. Potentially therefore one would expect an aberrant growth of such tissue, especially in the period of its greatest activity, the early months of pregnancy, to be highly malignant and destructive.

Chorio-epithelioma may thus arise if trophoblastic tissue takes on a malignant change. Marchand demonstrated the origin to be in the syncytium and Langhans layer of the villi. The growth may simulate villous structure, or it may be quite atypical in arrangement of the cells. While it may develop in association with early normal pregnancy or abortion, it is particularly liable to appear in association with or following hydatidiform mole. In many cases there is an interval of months or even years between the pregnancy and the appearance of the growth.

On account of the destructive and vascular character of the growth, uterine hemorrhage is an early symptom. Metastases occur through the venous channels and appear particularly in the vagina, vulva and lungs. X-ray examination of the chest may reveal pulmonary metastases. The Aschheim-Zondek test shows an unusually high concentration of the hormone and is of great value in diagnosis and prognosis. Unfortunately the clinical course of the growth is more conclusive proof of its malignant tendency than the microscopic examination, as spontaneous disappearance of the growth has been observed.

Accompanying the penetration of trophoblastic buds into the uterine decidua at a very early stage, vascularization of the future villi is effected through further differentiation of the trophoblastic layer, until the future placental area develops a rich circulation. Potentially therefore, in a tissue which is so highly vascularized, excessive capillary growth may occur, even to the extent of tumor formation. In this manner angioma of the placenta may arise.

In sectioning fixed placentas in strips from 0.5 to 1 cm. thick, I have found the characteristic firm, round

or oval encapsulated angioma only twice in examining about 2,000 specimens. While angiomas do not usually exceed from 1 to 2 cm. in diameter, much larger ones have been reported. The tumor may be shelled out of its pseudocapsule very much like a fibroid tumor of the uterus. Microscopically it is made up of innumerable small crowded capillaries, apparently within the confines of the stretched out Langhans and syncytial boundary of the original villus. Angioma is of no significance unless large enough to induce premature labor or possibly cause dystocia.

Conversely, if the villi fail to be vascularized or are insufficiently vascularized, degenerative changes of a hydropic nature may occur in the stroma and the lining cells which may possibly account for hydatidiform mole. One observes a similar tendency to edema of the villi, with the failing vascularity incident to syphilis of the placenta. In hydatidiform mole, however, the process is not a simple edema affecting the villous stem uniformly throughout but is a hydropic degeneration localized in a succession of enlargements along the course of the stem, giving rise to grapelike clusters of thin-walled cysts, which add immensely to the size and weight of the placenta and tend to loosen it from the uterine wall.

Embryonic growth is interfered with at a very early stage, and one seldom finds any trace of embryo or normal placental tissue. The Aschheim-Zondek test is strongly positive, because of increased concentration of the hormone. Enlargement of the ovaries, due to lutein cyst formation, frequently occurs and may be due to overstimulation of the anterior lobe of the pituitary gland from the excessive growth and degeneration of the epithelial elements of the villi. The enlargement subsides rapidly after expulsion of the mole.

The site of attachment and embedding of the fertilized ovum determines the location of the placenta in the uterus. While this is apparently largely a matter of chance, the vast majority of implantations are on the anterior or posterior wall of the fundus or body of the uterus.

Implantation in the lower uterine segment, resulting in placenta praevia, occurs much more frequently in multiparas. Is it not possible that the explanation of this lies in the fact that the anterior and posterior walls of the parous uterus are separated more than those of the virgin uterus, thus permitting the blastocyst to gravitate to a low level before embedding?

It would be of interest to compare the incidence of placenta praevia in a large series of cases in which the uterus is known to have been retroverted early in pregnancy with that in a like number of cases in which the uterus is known to have been in normal anteversion early in pregnancy.

Variations from the usual oval or round shape of the placenta probably result from lateral or cornual implantation. It is possible, however, that persistence of chorionic villi which unexpectedly survive their unfavorable location over the chorion laeve may account for some of the irregularly shaped placentas or the islands of placental tissue sometimes seen on the membranes and termed placenta membranacea.

During the second and third trimesters of pregnancy, with increasingly frequent and strong Braxton Hicks contractions and trauma, both from fetal movements within the uterus and stimuli from without, some of the outermost fastening villi at the margin of the placenta are probably torn from their decidual bed, thus

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causing repeated slight extravasations of blood at the margin of the placenta. The blood is prevented from extending inward beneath the placenta by the denser, more secure fastening villi or outward by the adherence of the membranes to the uterine wall. Consequently it follows the path of least resistance and bulges the chorion and amnion inward over the fetal surface of the placenta. This bulging fold of chorion and amnion, with its contained blood, is gradually flattened down onto the margin of the placenta by the intra-amniotic pressure.

After absorption of the hemoglobin the remaining fibrin creates the appearance of a thickened yellow border around part or all of the circumference of the placenta. This is, according to my observations, the probable mode of origin of circumvallate placenta. A section through the margin of such a placenta should show, from without in, (1) placenta, (2) chorion, (3) amnion, (4) amnion, (5) chorion, (6) fibrin, (7) chorion and (8) amnion. It is difficult, however, to identify and trace each of these layers in a specimen. The circumvallate border apparently opposes the further outward course of the vessels on the fetal surface of the placenta; these are seen to dip into the substance of the placenta at the inner margin of the circumvallate ring and continue their course within the placental substance to the extreme rim of the placenta, which in some cases extends several centimeters beyond the circumvallate ring.

In the last half of pregnancy certain changes occur in the placental arteries which play an increasingly important part, predisposing to hemorrhage and infarction. The basis for the vascular changes is the hypercholesteremia of pregnancy, which, from the early months on to term, is probably of fundamental importance to fetal growth.

Cholesterol, in the language of the biochemist, has been termed the framework of the body cell. If it is, there must be some mechanism by which the maternal organism mobilizes cholesterol to supply the excessive demands of cell growth in the fetus. It is thought that the pituitary gland governs cholesterol metabolism, and stimulation of the various functions of this gland by pregnancy may explain the mechanism by which the value for blood cholesterol increases from a normal one of from 150 to 170 mg. to an excessive one of from 200 to 250 mg. or more per hundred cubic centimeters. This value is still further increased if there is associated hypothyroidism or if the diet is particularly rich in cholesterol-containing foods.

Another factor, which, independently and also in conjunction with the hypercholesteremia of pregnancy, lays the basis for vascular changes in the placental arteries, is trauma produced by the increasingly vigorous movements of the fetal extremities on the unprotected vessels on the fetal surface of the placenta in the latter part of pregnancy. In respect to vulnerability, lack of support from surrounding tissue and subjection to direct trauma, the placental circulation is unique and unlike that of any other part of the body.

Under the combined influence of hypercholesteremia and fetal trauma, focal collections of lipid-like cells arise beneath the endothelium in some of the smaller placental arteries, probably at points where the vessel has been traumatized. I<sup>1</sup> noted the similarity in appear-

ance of these focal accumulations of lipid-like cells in the smaller placental arteries to the experimental cholesterol-induced vascular changes in rabbits and the spontaneously occurring vascular change accompanying coronary thrombosis in man, as shown by Leary.<sup>2</sup>

The accumulation of lipid cells beneath the endothelium and in the vessel wall may disturb the circulation in either of two ways. The lumen of the vessel may be gradually narrowed by bulging of the focus of lipid cells, which may finally shut off the circulation to the dependent villi, or the endothelium overlying the lipid cells may break down, either spontaneously or from the trauma of fetal movements, thus causing sudden thrombosis and loss of blood supply to the villi. Infarction necessarily follows, progressing rapidly in case of thrombosis or more slowly in case of mere narrowing of the lumen.

Areas of acute infarction in the placenta and their association with toxemia of pregnancy were first emphasized by Young.<sup>3</sup> He, however, considered them to be the result of interruption in the maternal blood supply, a view which cannot be reconciled with the sinusoidal character of the intervillous circulation. Manifestly, loss of maternal blood supply to any part of the placental site cannot deprive adjacent villi of maternal blood, which is free to reach this area from the surrounding intervillous circulation. Furthermore, villous vessels in the infarcted area are found to be thrombosed, indicating that the cause is on the fetal rather than the maternal side of the circulation.

Placental infarcts have been attributed also to the effect of some unknown toxic substance in the maternal circulation which causes localized degeneration of the villi. In view of the sharp line of demarcation between necrotic villi within the infarcted area and the surrounding healthy villi just beyond the border of the infarct, and the open intervillous circulation common to the two areas, it is inconceivable that any maternal poison circulating freely throughout the intervillous spaces would show a selective action on certain areas and not be uniformly harmful to all villi.

Failure to appreciate the relationship between placental infarcts and toxemia of pregnancy has been due to improper preparation and examination of the placenta and lack of familiarity with the more acute types of placental infarcts. The placenta should be wiped free of blood, the membranes cut away from the margin and the specimen fixed in 10 per cent solution of formaldehyde for from three to four weeks. It should then be cut in strips from 0.5 to 1 cm. thick, which are closely examined for evidence of infarction or hemorrhage.

Previous to 1937 I followed a routine of examining placentas in the light of a knowledge of the clinical history of each case. One cannot avoid being influenced in his interpretation of a suspicious area if he knows in advance whether or not the patient has had toxemia. During the past year all examinations have been made on "unknown" placentas, without a knowledge of the patient's clinical history at the time the placenta was sectioned. A definite diagnosis as to the occurrence of toxemia during the pregnancy has been made on the basis of the gross pathologic changes and then compared with the clinical diagnosis.

1. Bartholomew, R. A., and Kracke, R. R.: *Am. J. Obst. & Gynec.* **31**: 549 (April) 1936.

2. Leary, Timothy: Experimental Atherosclerosis in the Rabbit Compared with Human (Coronary) Atherosclerosis, *Arch. Path.* **17**: 453 (April) 1934.

3. Young, J.: *J. Obst. & Gynec. Brit. Emp.* **26**: 1, 1914; **34**: 279, 1927.

By this method it has been possible to arrive at a much more accurate classification of placental lesions and establish criteria and characteristics which differentiate the acute from the subacute or more chronic types. In a recent publication<sup>4</sup> placental infarcts were classified as A, B, C, D and E, listed in the order of increasing rapidity of infarction as well as in the order of increasing toxicity. The italicized letters indicate the infarcts which are associated with the increasing degrees of toxemia.

If infarction occurs rapidly the affected placental tissue appears as one or more round or oval areas

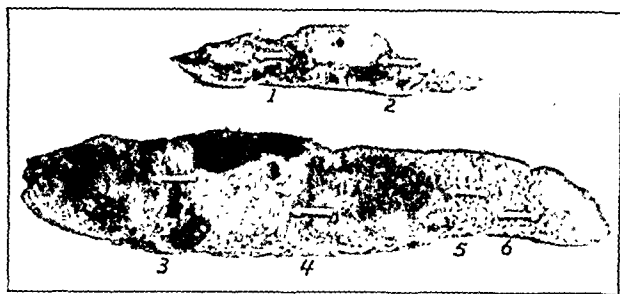


Fig. 1.—Placental strips from a primigravida, aged 21, who was normal at the twenty-seventh week of pregnancy but showed edema, slight albuminuria and a blood pressure of 150/82 at the thirtieth week, with no apparent increase at the thirty-second week. Two weeks later eclampsia and abruptio placentae developed; the blood pressure was 152/108 and increased to 170/130, and there was heavy albuminuria. Pregnancy was terminated and the patient recovered. Diagnosis from this placenta, sent from Dr. N. J. Eastman's service, Johns Hopkins Hospital, and examined as an "unknown," was as follows: Infarct C (1) and B (2) were probably responsible for a gradually increasing toxemia of several weeks' duration, followed by an acute exacerbation with severe toxemia and abruptio placentae due to early D (3), late D (4) and early E (5) infarcts. A late D infarct (4), with a superimposed blood clot, was responsible for the abruptio placentae. Infarct A (6) is nontoxic.

from 1 to several centimeters in diameter, which are sharply demarcated from the surrounding normal placental tissue by the color, which is a dark purple-black. These areas correspond to the distribution of the obstructed vessel. The consistency is still spongy and soft, as in normal placental tissue. When the strip is held toward the light the infarcted area preserves a granular-appearing surface. When the strip is bent the infarcted area bends as easily as the normal tissue. There may be a soft or a firm clot within or adjacent to the area. This type of infarct is designated as the early E infarct (figs. 1 and 2).

Microscopically, the stroma and lining cells of the villi show pyknosis and early karyolysis and are somewhat swollen, because of congestion of the villous capillaries. Many villous capillaries are thrombosed or show marked distention and rupture, with extravasation of fetal blood into the intervillous spaces, which accounts for the soft or firm clot. The intervillous circulation is freely open, there being no evidence of thrombosis.

Biochemically, placental tissue has been found to contain relatively more arginine than any other tissue.<sup>5</sup> Theoretically, in the process of autolysis of the infarcted area, guanidine may result from the breaking down of arginine<sup>6</sup> and, since guanidine is known to produce convulsions, the peculiar eclamptogenic nature of placental autolysate may thus be explained. Kracke, in testing the effects of injection of autolysates of various

tissues into animals to stimulate leukocytosis, has never observed convulsions, although toxic effects are evident.

Other poisonous protein split products resulting from placental autolysis are probably peptone and histamine. Peptone, if present in sufficient concentration, inhibits thrombosis through its anticoagulant effect. This tends to keep the intervillous circulation open and permits absorption of the poisons into the maternal circulation. The known effects of these products explain practically all the clinical and pathologic manifestations of toxemia of pregnancy.

Clinically, the acute type of infarction is associated with the more acute, fulminating, preeclamptic, eclamptic or abruptio placentae type of toxemia, and there is a direct relation between the amount of tissue involved and the severity of the toxemia. It is usually found when the patient progresses from a normal state to preeclampsia, eclampsia or abruptio placentae within a week or ten days.

If infarction is slightly older or less acute (late E infarct, fig. 2) the lesion is still dark or purple-black but has changed from a spongy to a more compact firm area, sharply demarcated from the surrounding lighter spongy tissue. It is firmer to palpation, and when the strip is held toward the light the surface of the lesion appears marble-like and shiny. When the strip is bent, the infarcted area either cracks sharply or holds together and does not bend with the rest of the strip.

Microscopically, the villi show pyknosis and some degree of karyolysis and karyorrhexis. Some of the distended villous capillaries are ruptured and the extravasated blood, with tissue debris, fuses the villi and causes the area to appear more compact. There is still open intervillous circulation, which disseminates poisonous protein split products of placental autolysis. Clinically, the toxemia is almost if not quite as fulminating as that associated with the early E infarct, but there may be opportunity to induce labor before abruptio placentae or eclampsia occurs.

If infarction is still less acute or of longer duration, corresponding to a clinical course of from two to three

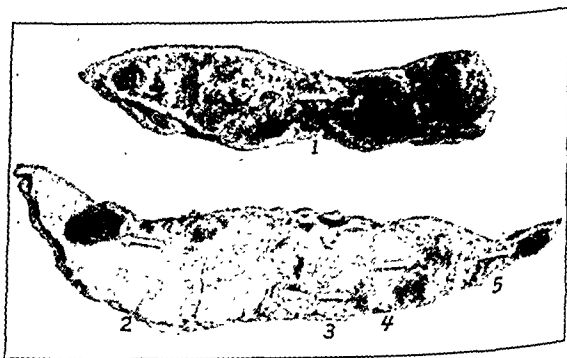


Fig. 2.—Placental strips 3 and 4 were obtained from patients with eclampsia and preeclampsia, respectively. The arrows point to two late E infarcts (1) and early E infarcts (2, 3, 4 and 5).

weeks, the infarcts vary from a faint brown (early D) to a definite brown (late D), as seen in figure 1, and are sharply demarcated, firm, compact, smooth and shiny and hold together when the strip is bent. Microscopically, the blood cells, both maternal and fetal, are more degenerated and stain more faintly, the change in the hemoglobin accounting for the brown color. The villi show more necrosis and disintegration. The inter-

4. Bartholomew, R. A., and Colvin, E. D.: Tr. Am. Gynec. Soc., June 1938; Am. J. Obst. & Gynec. 36: 909 (Dec.) 1938.  
5. Harding, V. G., and Fort, C. H.: J. Biol. Chem. 35: 29 (July) 1918.  
6. Bartholomew, R. A., and Parker, Francis: Am. J. Obst. & Gynec. 27: 72 (Jan.) 1934.

villous spaces are still open and permit free absorption of toxic autolytic products.

In a series of 100 placentas, from both normal and toxic patients, examined as "unknowns,"<sup>4</sup> there were twenty which suggested severe toxemia, classified clinically as preeclampsia, eclampsia and abruptio placentae. The presence of early and late types of infarcts *D* and *E* made it possible to make a correct pathologic diagnosis in 90 per cent of the cases.

If infarction is even slower the lesion, designated as infarct *C* (fig. 1), appears as a brown-yellow, sharply demarcated area and may show some softening or breaking down. Microscopically, the villi stain poorly or not at all and show considerable disintegration. The intervillous circulation is sufficiently open to permit absorption of toxic products, but there is considerable intervillous thrombosis in some parts of the infarct. Clinically, infarct *C* is associated with toxemia of a more gradual but progressive type, extending over a period of four or five weeks. Induction of labor may be necessary.

Infarct *B* (fig. 1) is a slow-forming, yellow-white, firm, sharply demarcated lesion and is apparently due to gradual obliterative endarteritis or slow occlusion from cholesterol-induced vascular change. Since the small arteries are more often affected, the infarct is usually found on the margin of the placenta.

Microscopically, the villi are pale and stain faintly but preserve their normal outline. There is no disintegration. The thrombosed intervillous blood has been changed to a dense homogeneous pink-staining hyaline substance, but in some areas there is still slight intervillous circulation. The yellow color of the lesion is due to scattered areas of incomplete thrombosis, containing shadows of degenerated red cells and some active necrosis of the villi, which permit slight absorption of toxic products.

Clinically, infarct *B* is associated with very mild manifestations of toxemia. The patient may have had slight edema, a trace of albumin and a slight rise in diastolic blood pressure, to 80 or 85, but there has been no tendency to increased toxemia unless a new area of more acute infarction occurred.

Infarct *A* (fig. 1) is firm and sharply demarcated and appears identical with infarct *B* (fig. 1) except that it is white. The absence of yellow color is due to complete hyalinization of the intervillous blood which surrounds the pale "ghost villi." Since the etiologic factor is slow obliterative endarteritis in a terminal artery, infarct *A* is usually on the margin of the placenta. It is nontoxic, not only because of the complete hyalinization of the intervillous blood but also because of the slow necrosis of the affected villi.

Lesions *A*, *B*, *C*, *D* and *E* are true infarcts characterized by progressive increase in the rapidity of infarction. Grossly, the more rapid the infarction the less conspicuous the lesion, the less firm the consistency, the darker the color and the greater the toxicity. Microscopically, the more rapid the infarction the less apparent the intervillous thrombosis and, except in the most acute stage, the greater the disintegration and loss of staining power of the villi. The range in color, due to change in the hemoglobin, is from very dark purple-black in infarct *E* to brown in *D*, to brown-yellow in *C*, to yellow-white in *B* and to white in *A*. The size and number of the infarcts bear a definite relation to the severity of the toxemia.

Simple hemorrhage without associated infarction may also occur in the placental substance. Since there can be no hemorrhage in a sinusoidal circulation such as the intervillous circulation, the probable source of such hemorrhage, when there is no associated infarction, is simple rupture of the capillaries of a terminal villus, resulting in extravasation of fetal blood. The villi are forcibly pushed aside and compressed about the margin of the hemorrhage.

Whether the collection of blood is absorbed and drained away completely, leaving an excavated open area, or whether a blood clot remains and passes through the stages from dark to brown clot and finally to white or yellow fibrin probably depends on the compatibility of the maternal and fetal blood. A slight degree of incompatibility may account for the soft transparent gelatinous areas which are occasionally seen in the placental substance. Shadows of red cells or a slight pink color give evidence of a hemorrhagic origin of these areas.

A layer of compressed villi about a recent hemorrhage may simulate an acute infarction, particularly if there is some infiltration of dark blood into the villi beyond the hemorrhage, thereby giving to the area a dark color. The lesion, however, is diffuse and not sharply demarcated. Microscopically, the villi do not show necrosis. If the clot is yellow or white the evident age of the hemorrhage argues against an associated acute infarction and the compressed border of the lesion is of a lighter color owing to crowded villi and diminished intervillous blood.

The cause of simple hemorrhage in the placental substance is obscure, but it seems reasonable to believe that temporary pressure on the thin-walled umbilical vein through certain movements or positions of the fetus in the late months of pregnancy may cause sufficient distention of a terminal villous capillary that rupture may occur.

Small collections of yellow-white fibrin varying from 0.5 to several centimeters in diameter are frequently seen on the fetal surface of the placenta beneath the chorion. The origin of these lesions is undoubtedly rupture of small branches of the umbilical arteries from the trauma of fetal movements. They are occasionally of immense size, indicating sudden extravasation from rupture of a large artery.<sup>7</sup> Cysts on the fetal surface of the placenta undoubtedly arise from liquefaction of a localized hemorrhage.

The circulatory disturbances thus far described concern pathologic changes in the placental arteries. I believe that the rare fetal anomaly termed general edema of the fetus, concerning which Ballantine wrote a monograph, is due to occlusion of the umbilical vein at some point between its origin at the placental end of the cord and its tributaries in the liver within the body of the fetus. The condition is associated with a high incidence of toxemia and marked increase in size of the placenta, which appears pale, white and extremely edematous. The villi show marked edema and early degenerative change due to slowing or arrest of the circulation. Since the entire placenta is involved, the toxemia is acute and severe. There is urgent need to investigate cases of general edema of the fetus, particularly from the standpoint of this probable etiologic factor. The frequency of fetal blood dyscrasia, with

7. Bartholomew, R. A., and Kracke, R. R.: *Am. J. Obst. & Gynec.* 24: 797 (Dec.) 1932.

excessive numbers of megaloblasts, emphasizes the importance of a complete study of the blood.

Finally, local or general infection of the placenta may occur by way of the genital tract or through the maternal blood stream. Pyogenic infection is practically always postabortal and ascending by way of the genital tract. Portions of the decidua and the adjacent intervillous spaces show thrombosis and numerous polymorphonuclear leukocytes. Invasion of the fetal circulation by the organisms, and intra-uterine fetal death, while apparently rare, may prove to be more frequent than suspected with closer study of the placenta and improved methods of isolation of bacteria from the fetus.

Tuberculous infection of the fetus is necessarily transplacental and is generally believed to be preceded by definite tuberculous lesions of the placenta. The demonstration of tubercle bacilli may require thorough search by histologic and inoculation methods. However, the finding of tuberculous lesions in the placenta does not invariably mean that the fetus is infected.

Syphilis of the placenta, contrary to statements frequently made in the literature and textbooks, is not recognizable by a specific appearance of the gross specimen and is not always suggested by undue size of the placenta. Microscopically, in the more mature placentas of the last trimester of pregnancy the villi appear large, somewhat crowded and edematous. The stroma shows rather loose open structure, and the vessels of the villi are inconspicuous in number and size and show round cell infiltration. Spirochetes are demonstrated with much more difficulty in the placenta than in the fetus. A positive histologic appearance is strong evidence of syphilis but is not regarded as positive proof.

Since the placenta apparently functions as a rather efficient barrier to transplacental infection of the fetus, some experiments were carried out by Kracke to determine if possible whether placental extract, in comparison with other tissue extracts, possesses some bactericidal power or inhibiting influence on bacterial growth when used as a culture medium. Contrary to the anticipated result, it was found to be a good culture medium for the commonly occurring bacteria and an excellent medium for streptococci.

#### CONCLUSIONS

1. Infarction of the placenta is the most important pathologic condition to which this organ is subject, not only from the standpoint of frequency but also because of its relation to toxemia of pregnancy and maternal and fetal mortality.

2. The predisposing causes of placental infarction are, first, the hypercholesteremia of pregnancy, which favors the accumulation of lipid cells at points of stress or injury of the placental arteries, similar to that seen with coronary occlusion, and, secondly, the trauma of fetal movements, which not only tends to cause deposits of lipid cells at points of injury to the placental arteries but also may break the endothelium over such a deposit or actually bring about rupture of the vessel, thus causing rapid thrombosis.

3. Toxemia of pregnancy probably results from the absorption of poisonous protein split products of placental autolysis.

4. The poisonous products of placental autolysis are probably peptone, histamine and guanidine. The patho-

logic effects of these poisons satisfactorily explain the symptoms and pathologic changes of toxemia of pregnancy.

5. The peculiar eclamptogenic character of placental autolysate is probably explained by the higher content of arginine in placental tissue, from which guanidine may be obtained.

6. Toxemia of pregnancy is associated with definite types of acute infarction of the placenta. In examining "unknown" placentas it is possible to diagnose pre-eclampsia, eclampsia or abruptio placentae in 90 per cent of the cases.

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#### ABSTRACT OF DISCUSSION

DR. A. J. CARLSON, Chicago: I presume these placentas were taken in a routine manner. Did you examine all the placentas?

DR. BARTHOLOMEW: That is right.

DR. CARLSON: What is the amount of guanidine in the urine in these patients? There have to be considerable amounts in the blood to get these symptoms. What about the pathologic conditions in the liver that have been described in these eclamptic patients? Do you describe them as secondary effects of these poisons from the placenta?

DR. FRANK W. HARTMAN, Detroit: I had the privilege a few years ago of reviewing a thousand consecutive placentas at our hospital, and we found over 50 per cent of infarcts. We were unable to correlate in any way the number or size or occurrence of these infarcts with toxemias in this group of cases. I wonder if the infarcts in the placenta aren't the result of the same thing that produces the liver lesions and other lesions throughout the body rather than that the infarcts produce the chemical changes that are the initial cause. There is some substance which produces the spasm, perhaps, of the vessels, and the infarcts in the placenta, and the hypertension and the changes in the liver. It has been shown that one of the best ways to reproduce these lesions in the liver is to place animals under partial oxygen tension for several days, and under those conditions of anoxia the liver does show lesions very close to the lesions seen in the toxemia of pregnancy. Another condition in which similar facts have been blamed for shock and death is extensive burns. There the blood pressure goes in the opposite direction, it usually falls, and the patient dies from vascular collapse and shock. They frequently show lesions in the liver which are very similar to what are seen in eclampsia.

DR. R. A. BARTHOLOMEW, Atlanta, Ga.: With regard to whether guanidine is present in the urine, we have not finished some work that has recently been undertaken, namely, taking an equal weight of placenta and liver or spleen, and subjecting both tissues to autolysis to determine if possible whether there is a greater amount of guanidine obtainable from placental tissue. Major, I believe, has demonstrated an increased amount of guanidine in the urine of eclamptic patients and Titus has produced convulsions and eclamptic-like lesions in the liver and kidney of rabbits by injections of guanidine. In the early part of the work guinea pigs were injected with autolysate of human placenta which had autolyzed as little as four or five hours, and daily injections over a period of eight or ten days resulted in the production of typical eclamptic convulsions and a pathologic condition of the liver and kidney similar to that seen in eclampsia. I emphasized particularly that acute placental infarcts are sharply circumscribed and that the intervillous circulation in the infarcted area is widely open, permitting maternal blood which circulates freely in the adjoining healthy placenta to circulate between the necrotic villi of the infarcted area. The acute infarcts cannot be explained on the basis of a hypothetic poison in the maternal blood. Such a poison would have a uniformly lethal effect on all villi and not a selective effect in certain areas of the placenta. This, in my opinion, indicates that the infarct and its poisons are primary in the placental tissue and not in the mother's blood.

THE USE OF POTASSIUM SALTS  
IN HAY FEVER

PRELIMINARY REPORT

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The present study was stimulated by the thought that allergy is, in great part, a disturbance of electrolyte metabolism. Analogy could be drawn between demonstrated electrolyte disturbances in other diseases, such as thyroid disease (iodide), parathyroid disease (calcium), Addison's disease (sodium and potassium) and the potassium alterations that have been described in diabetes.

Cook and Stoesser<sup>1</sup> treated asthmatic children with "salt-free" diets and injections of pitressin and found that, in spite of the antidiuretic action of the pitressin, there was an increased, rather than a decreased, excretion of the sodium ion and that with this there was a distinct relief of the asthma. In one patient asthma was seemingly reinduced by the administration of a large dose of sodium chloride. This experimental work also suggests the importance of the water balance in asthma, comparable to its importance<sup>2</sup> in Addison's disease. Clinically, Piness<sup>3</sup> has stressed the importance of the need for water by patients with status asthmaticus, and he therefore administers it by various routes in copious amounts in these cases. Davis<sup>4</sup> has had remarkable success in the treatment of chronic asthma by a regimen an important part of which is the free use of water enemas.

In the article by Rusk and Kenamore<sup>5</sup> the excellent suggestion was made that urticaria might be an expression of localized edema which might respond to the action of a diuretic. They used potassium chloride and found it thoroughly effective in six cases of severe urticaria. They quote Nathan and Stern<sup>6</sup> as saying that in the acute dermatoses serum potassium fell to a subnormal level and returned to normal as the cutaneous lesions improved.

It has been demonstrated that the pharmacologic action of potassium chloride is, in many respects, similar to that of epinephrine. Seager,<sup>7</sup> however, could not verify this similarity in the iris of the frog. In addition, in my own experiences with potassium chloride none of the usual side-effects of epinephrine or ephedrine were observed in the doses used (the highest dose being 50 grains [3.2 Gm.] in twenty-four hours), in spite of its effectiveness and at times surprisingly rapid action. Rusk and Kenamore state that "effects attributed to epinephrine are actually the effects produced by potassium migration which epinephrine causes." This would readily explain the well known ineffectiveness of epinephrine in status asthmaticus after repeated, frequent

doses have been given. In other words, epinephrine liberates potassium from the tissues, and when the tissues are sufficiently depleted epinephrine can no longer relieve the symptoms of allergy.

CLINICAL RESULTS

This preliminary report deals mainly with the use of potassium salts in a number of patients with hay fever. The clinical results shown in the accompanying table appear to be so conclusive that lengthy, detailed reports of cases will be omitted.

The method of administration proved to be simple. In one of the first cases in which potassium chloride was tried it was given as a 10 grain (0.65 Gm.), enteric coated capsule. This produced agonizing epigastric pain five minutes after administration and later, when it was found that other patients complained of vague

The Effect of Potassium Salts on Hay Fever and Pollen Asthma \*

Case	Age	Sex	Diagnosis	Severity	Relief Obtained
1. M. T.....	36	♀	Hay fever	+++	++++
2. P. B.....	39	♀	Hay fever	+++	++++
3. E. R.....	24	♀	Hay fever	++	++++
4. E. S.....	44	♀	Hay fever	+++	++++
5. F. B.....	38	♀	Hay fever	+++	++++
6. W. C.....	42	♀	Hay fever	++	++++
7. R. W.....	43	♀	Hay fever	+++	++++
8. S. W.....	44	♀	Hay fever	+	++++
9. W. P.....	41	♀	Hay fever	+	++++
10. M. R.....	40	♀	Hay fever	++++	+++
11. D. W.....	18	♀	Hay fever	+	+++
12. M. M.....	40	♀	Hay fever	++++	++++
13. W. R.....	38	♀	Hay fever	++	+++
14. E. R.....	37	♀	Hay fever	++++	++++
15. L. W.....	30	♀	Hay fever	+++	++++
16. J. B.....	16	♀	Hay fever	+++	++++
17. L. G.....	37	♀	Hay fever	++	++++
18. D. M.....	42	♀	Hay fever	+	++++
19. B. D.....	40	♀	Hay fever	+++	++
20. M. L.....	31	♀	Hay fever	++++	++++
21. B. B.....	37	♀	Hay fever	+	++++
22. O. H.....	44	♀	Hay fever	++++	++++
23. F. N.....	38	♀	Hay fever	++	++
24. A. A.....	33	♀	Hay fever	+++	+++
25. J. T.....	12	♂	Hay fever and asthma	++++	++++
26. S. L.....	32	♀	Hay fever and asthma	+	++++
27. E. M.....	12	♂	Hay fever and asthma	+++	++
28. F. I.....	28	♀	Hay fever and asthma	+++	++
29. S. Q.....	19	♀	Hay fever and asthma	++	++++

\* Most of these patients were originally treated with 5 grains of potassium chloride three times a day; in a few cases four doses were given; the most that one patient received was 50 grains (3.2 Gm.) a day. The doses for children and the elderly must be worked out.  
† These patients had had nearly adequate relief from desensitization.

abdominal distress, it was decided to give it in 5 grain (0.32 Gm.) doses dissolved in a glass of water. This illustrates the need for extensive studies on the toxicity of potassium salts, although the latter procedure proved to be entirely satisfactory. Later, when it was felt necessary to prove that the clinical effect came not from potassium chloride as such but from the potassium ion, a mixture of potassium salts in solution was prescribed, and this was found to be almost equally effective. This solution of potassium salts contained 3½ grains (0.2 Gm.) each to the drachm (4 Gm.) of potassium acetate, potassium bicarbonate and potassium citrate. Rusk and Kenamore experienced no real difficulty with the use of 15 grain enteric coated capsules, but in view of my experience I would recommend that these salts be given in dilute solution. A 5 grain powder of potassium chloride dissolved in a glass of water is practically tasteless.

Read at the regular meeting of the Pima County Medical Society, Nov. 15, 1938.  
Dr. Solomon Strouse, Los Angeles, and Dr. Donald F. Hill, Tucson, encouraged and assisted in this work.  
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2. Personal communication to the author from Dr. H. H. Cutler, Rochester, Minn.  
3. Personal communication to the author from Dr. George Piness, Los Angeles.  
4. Personal communication to the author from Dr. W. Claude Davis, Tucson, Ariz.  
5. Rusk, H. A., and Kenamore, B. D.: Urticaria: A New Therapeutic Approach, *Ann. Int. Med.* 2: 1838 (April) 1938.  
6. Nathan, E., and Stern, F., quoted by Rusk and Kenamore.  
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*Hay Fever.*—Altogether twenty-nine cases of hay fever, six with pollen asthma, were studied during the Tucson fall hay fever season, the common offenders at that time being false ragweed, careless weed (amaranth) and bermuda grass. The symptoms varied in severity from slight sneezing and nasal discharge to severe hay fever symptoms and, in the six cases, asthma. Most of the patients responded quickly to 5 grains of potassium chloride given three times a day, some experiencing relief within a few minutes and some in about a half hour. Others, whose hay fever was mostly nocturnal, reported the next day that they had had much better nights. In only one case did an increase of symptoms follow an initial improvement, and this patient obtained adequate relief after the dose was increased to 25 grains (1.6 Gm.) of potassium chloride a day.

In one family of four, all of whom had severe hay fever, the two who were given the medicine responded; the other two continued to have hay fever. In another family of three sisters, all with severe hay fever, the one who was given the medication obtained complete relief; the other two continued to have severe hay fever. In the series of hay fever cases control studies by substituting inert medication were not carried out. One patient had a return of symptoms within twelve hours after he stopped taking his medicine and was again relieved as soon as it was resumed. In one case the medication was experimentally stopped and symptoms returned the following day; medication was resumed after three days and the symptoms disappeared satisfactorily. In a few instances, patients neglected to take their potassium chloride regularly and found that the omission of one dose resulted in a recurrence of symptoms, usually in from five to eight hours.

As is indicated in the table, every one of the patients experienced a degree of relief which in all cases was estimated as over 50 per cent and in most of them approximated 100 per cent. The first improvement noticed was the disappearance of irritation of the eyes. Within twenty-four hours the copious nasal discharge had almost entirely cleared. For about another day a few of the patients persisted in having a rare attack of dry sneezing. By the third day the patients who in the table are graded as having a 4 plus relief were free from symptoms. With the disappearance of sneezing and discharge, which in many cases interfered with sleep, the general state of health of these patients was greatly improved.

The following report illustrates the striking effect of potassium chloride in a severe case:

J. T., a boy aged 12 years, had had hay fever and asthma for the past eight summers, during the last four of which considerable relief had been obtained by desensitization with an allergen mixture. Injections had been omitted the past summer because of the illness of the patient's physician. The summer was spent on the Pacific coast, where the boy was practically free from symptoms. On returning to Tucson, however, during the ragweed and careless weed seasons, hay fever and then asthma started, and as these increased in severity diarrhea, abdominal cramping and then vomiting set in. In ten days the boy lost 15 pounds (6.8 Kg.). The patient could have been treated with epinephrine and ephedrine, or he could have been moved into a pollen-free atmosphere. It was decided, however, to try potassium chloride. The first dose was immediately regurgitated; half an hour later another dose was given and from that time on there was no sneezing, wheezing or vomiting. By the next day the cramping and diarrhea had disappeared. The medication was continued in 5 grain doses three times a day. At the end of a week he had regained about 10 pounds (4.5 Kg.) and felt fine.

The only complicating factor in this series was in case 28. This patient had not only hay fever and asthma but also urticaria, rheumatic heart disease and a long-standing, persistent, mild arthritis. This patient became entirely free from hay fever and asthma for two days but then had recurrent asthma and urticaria thought to be due to food sensitivity. This case will be reported in detail later.

Chemical studies of blood and urine, which had been done on the chronic asthmatic patients and which will be reported later, were not made in this group of hay fever patients.

*Chronic Asthma.*—The original studies on this phase of allergy were made on a group of ten patients with chronic persistent asthma. It is important to note that in none of them did any improvement occur from potassium chloride. Studies on these patients are being continued and will not be reported here in detail. It is sufficient to say that I have found in these cases that a "salt-free" diet seemingly decreases the severity of the asthma and that, furthermore, the administration of potassium iodide during the period of the "salt-free" diet practically eliminates severe asthmatic attacks. The beneficial effect thus obtained seems to be greater than would be obtained by the use of a "salt-free" diet or of potassium iodide alone. It should be made clear that these patients are, in general, not cured, although some of them are much better than they were before treatment was started.

*Other Allergic Diseases.*—In view of the excellent results obtained with hay fever it was thought advisable to record the results obtained in a small number of cases of other allergic diseases. Three cases of urticaria, two chronic and one acute, responded favorably to 5 grain doses of potassium chloride given three times a day. The skin in one case of long-standing thickly encrusted eczema was almost cleared in five days, leaving at that time only a brown-red discoloration to the smooth skin. In another case a mild eczematoid, itching lesion of the forearms disappeared in three days. Three patients with chronic sinusitis, apparently allergic, reported decrease of discharge and pain. In one of these acute severe frontal and antral pain completely disappeared in three minutes. In one patient with nasal polyps which had completely blocked the passage of air on both sides for three weeks, opening of the air passages occurred within an hour after a 5 grain dose of potassium chloride. The patient had expected to have nasal polyps removed, as had been done in the past, but has had practically no nasal blocking since this one simple experiment was tried three months ago. A Negro woman with nasal polyps completely blocking both nares was kept on potassium chloride 5 grains three times a day for two weeks, at the end of which time the polyps on the left side were seen to have partially shrunk, so that the anterior third of the left naris was free. One week later the left naris was sufficiently open to permit the passage of air. The results in these two cases encourage the belief that even severe nasal polyposis does not inevitably require surgery. In another instance, in which nasal polyps had recently been removed, potassium chloride was given and after two days the patient noticed marked freeing of the air passages. Dr. John Mikell, nose and throat specialist, who was unaware of the nature of the medication or of its mode of action, found at this time that the edema of the inferior turbinate had completely disappeared. In three typical cases of migraine relief

was obtained in only one, and this occurred within four hours after 20 grains (1.3 Gm.) of the potassium salt mixture was given. In two other cases no effect was produced with 15 grain and 30 grain (1 and 2 Gm.) doses of potassium chloride respectively.

It must be emphasized that these results are in no way to be considered conclusive. They are reported here only because, in some instances, various allergic disturbances seem to respond to potassium salt therapy.

*Food Sensitivity.*—A simple clinical experiment was tried on a man aged 44, who had for years regularly had acute nasal blocking (from polyps) and severe hives following the ingestion of shrimp, beer, candy in large amounts, or a combination of tomatoes and sugar, for each of which substances he had a penchant. He was asked to eat a portion of shrimp after taking 5 grains of potassium chloride. In his enthusiasm for the experimental method he took not only a large portion of shrimp but also a glass of beer, some tomatoes and sugar and then a large quantity of candy. No hives appeared but some rhinitis did develop, which was quickly relieved by the second dose of the medicine. The following morning he ate three tablespoonfuls of jam, which had also always given him hives and nasal blocking but which this time produced no symptoms at all.

#### COMMENT

From the results obtained in this study, as well as those reported by Rusk and Kenamore, it seems that potassium plays an important role in the mechanism of allergy. Obviously other electrolytes, including sodium, calcium, chloride and iodide, take part in this complex disturbance. Much recent work has shown the importance of altered electrolyte metabolism in endocrine disturbances, and it may well be that allergy is basically an endocrine dysfunction with secondary disturbances of electrolyte metabolism. This hypothesis, however, remains to be demonstrated. In view of the good results obtained in a few cases of asthma and eczema, with adrenal cortex extract, and in view of the known relationship in Addison's disease of the adrenal cortex to sodium and potassium disturbance, it seems probable that it is the adrenal gland that is primarily involved. Because of the well established relationship of epinephrine to allergic manifestations it would seem that this disturbance of the adrenal gland involves the medulla as well as the cortex.

This concept of allergy, indicating that the major disturbance is one of altered electrolyte metabolism, immediately suggests that the proteins produce manifestations only when the underlying electrolyte mechanism is disturbed.

It has been shown in this study that a much neglected simple inorganic chemical compound is of considerable importance not only in therapy but also in the study of a complex group of disturbances. It is hoped that this work will stimulate others whose facilities are more adequate.

#### CONCLUSIONS

1. Striking benefit was obtained from the use of potassium salts in twenty-nine cases of hay fever. These salts are also used in urticaria, eczema, nasal polyposis, chronic allergic sinusitis and migraine.

2. In chronic asthma potassium chloride is apparently ineffective; the use of potassium iodide, however, in combination with a salt-poor diet, seems helpful but not curative.

3. The method of administration of potassium salts is simple; no complication or "side effects" were noted, although further studies of toxicity are needed.

4. It is suggested that allergy is predominantly a disturbance of electrolyte metabolism associated with some endocrine (possibly adrenal) dysfunction.

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## TOXIC HEPATITIS DUE TO SULFANILAMIDE

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Although numerous toxic effects of sulfanilamide have been described, there are only a few references in the literature to damage to the liver produced by this drug. Hageman and Blake<sup>1</sup> have observed one case of toxic hepatitis presumably due to sulfanilamide. This patient recovered promptly when the drug was discontinued. Saphirstein<sup>2</sup> has recorded a severe but nonfatal case of toxic hepatitis caused by sulfanilamide. In this instance there was an associated exfoliative dermatitis.

Two deaths from hepatitis following the use of sulfanilamide have been reported by Bannick, Brown and Foster.<sup>3</sup> They felt that possibly their patients suffered hepatic damage prior to the beginning of the treatment and concluded that sulfanilamide may cause preexisting hepatic damage to progress to a stage from which regeneration is impossible. In contrast to this complication they have seen mild attacks of jaundice, which usually subsided rapidly when use of the drug was discontinued and intake of fluids was forced.

Long<sup>4</sup> in his experience with sulfanilamide has encountered jaundice with marked decrease of hepatic function on only one occasion. He believes that previous hepatic damage or jaundice is not necessarily a contraindication of sulfanilamide therapy.

This communication reports five cases of toxic hepatitis apparently caused by sulfanilamide, and increases the evidence that this drug is capable of causing severe damage to the liver.

CASE 1.—N. M., a white man, aged 25, who entered the Cleveland City Hospital Nov. 6, 1937, complained of a cutaneous disorder.

October 16 he had been started on a course of sulfanilamide as treatment for gonorrheal prostatitis. No other medication was administered. October 29 the patient had a chill followed by a fever of 38.5 C. (101.3 F.). The sulfanilamide was discontinued at once, a total of 50 Gm. having been given. November 4 a generalized cutaneous eruption appeared, and the patient became acutely ill. He entered the hospital two days later.

Examination showed the cutaneous eruption to consist of confluent red maculopapules with a few minute vesicles and pustules. General examination was otherwise negative except that the temperature was 38 C. (100.4 F.) and the liver and spleen were just palpable. Within the next few days the cutaneous eruption became more severe and icterus appeared. The edge of the liver was now 5 cm. below the costal margin.

From the Department of Medicine of Cleveland City Hospital and the Western Reserve University School of Medicine.

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On the third hospital day, the urine contained both bile and urobilinogen, and the icteric index was 63. On the sixth hospital day examination of the blood revealed sulfanilamide 0.2 mg. per hundred cubic centimeters, urea nitrogen 13 mg., sugar 83 mg., cholesterol 232 mg. and phosphatase 15.6 mg. The leukocytes numbered 19,000 per cubic millimeter and the erythrocytes 4,200,000. The hemoglobin was 12.1 Gm. per hundred cubic centimeters and a smear of the blood was normal. The Kline test for syphilis was negative.

During the next week the patient became deeply jaundiced, stuporous and very ill. The temperature varied between 38 and 40 C. (100.4 and 104 F.), the respiratory rate between 30 and 40 per minute and the pulse rate between 100 and 130 beats per minute. The cutaneous eruption progressed into a typical exfoliative dermatitis. The edge of the liver was now 10 cm. below the costal margin and the abdomen was distended with fluid. The urine contained large amounts of bile and urobilinogen, and the stools were light in color.

The therapy during this period consisted of a high carbohydrate-low fat diet, insulin, intravenous dextrose, blood transfusion, forced fluids, emollients and symptomatic treatment. On the thirteenth hospital day the patient began to improve. The temperature returned to normal. The fluid in the abdomen absorbed rather rapidly. The icterus slowly decreased, as did the bile and urobilinogen in the urine. The skin and the liver gradually returned to normal, and the patient was discharged on the thirty-eighth hospital day.

CASE 2.—G. B., a Negro woman aged 24, who entered the Cleveland City Hospital April 5, 1938, had received 33 Gm. of sulfanilamide from February 28 to March 10 inclusive for an infection of the pelvis. The patient then changed physicians and on March 16 received a single 0.6 Gm. dose of sulfanilamide, which caused her to have fever. Again on March 26 she received another 0.6 Gm. dose of sulfanilamide. No other medication was given. Following the last dose of sulfanilamide the patient's temperature varied between 38.5 and 39 C. (101.3 and 102.2 F.). March 30 she became icteric and the urine contained bile. The following day a generalized dermatitis appeared and thereafter the patient became acutely ill, entering the hospital five days later.

Examination showed a generalized exfoliative dermatitis and moderate jaundice. The edge of the liver was palpable 10 cm. below the costal margin. There was moderate thickening of both fallopian tubes. The urine contained bile grade 4 plus and urobilinogen grade 2 plus. The icteric index was 69. The erythrocytes numbered 2,500,000 per cubic millimeter, the leukocytes 30,000 and the value of the hemoglobin was 50 per cent. A differential count showed the leukocytes to be 50 per cent lymphocytes. The Kline test for syphilis was negative.

Therapy consisted of forcing fluids, high carbohydrate-low fat diet, intramuscular liver, ferrous carbonate by mouth, insulin, intravenous dextrose, blood transfusion and symptomatic treatment, but the patient became progressively worse and died April 10, on the fifth hospital day. Permission for a postmortem examination was not obtained.

CASE 3.—G. D., a white man aged 41, entered the Cleveland City Hospital Dec. 14, 1937, because of erysipelas of two days' duration. The patient said that he had drunk about 1 quart (liter) of whisky daily for the past fifteen years, although he had not taken any for a few days prior to his admission to the hospital.

Except for the erysipelas, the general physical examination was negative and sulfanilamide therapy was begun. No whisky or other medication was administered. On the third hospital day it was noted that the edge of the liver was 2 cm. below the costal margin. The sulfanilamide accordingly was discontinued at once, the patient having received a total of 26 Gm. The blood sulfanilamide was 15 mg. per hundred cubic centimeters. On the sixth hospital day the edge of the liver extended 6 cm. below the costal margin. The patient was jaundiced and the urine contained bile grade 4 plus. The stools were not acholic and the spleen could not be palpated. At this point the patient started to improve. The erysipelas and jaundice cleared rapidly and the liver decreased in size, the patient being discharged on the fifteenth hospital day.

Repeated blood studies showed no abnormalities except for leukocytosis at the time the erysipelas was present. The Kline test for syphilis was negative.

CASE 4.—T. J., a white man aged 40, who entered the Cleveland City Hospital Oct. 4, 1937, had received 35 Gm. of sulfanilamide from September 17 to October 3 inclusive because of chronic prostatitis. No other medication was administered. Two days before the sulfanilamide was discontinued the patient noted jaundice and vague epigastric pain.

General physical examination was negative except that the skin was moderately icteric and the liver extended 3 cm. below the costal margin. The urine contained large amounts of bile. Examination of the blood revealed the icteric index 63, phosphatase 18.1, phosphorus 2.6 mg. per hundred cubic centimeters, cholesterol 142 mg., sugar 83 mg., urea nitrogen 13 mg. The Kline test for syphilis was negative.

The jaundice gradually increased until the ninth hospital day, when the icteric index was 160. At this time the edge of the liver was 8 cm. below the costal margin. Thereafter the icterus slowly decreased and the liver returned to normal size, the patient being discharged November 9 in good health on the thirty-sixth hospital day. He was not seriously ill at any time nor did any anemia appear. Cholecystograms taken November 19 (ten days after discharge) were negative.

CASE 5.—T. M., a Negro aged 28, entered the Cleveland City Hospital Aug. 4, 1937, because of second degree burns of the left hand and left leg. In order to combat secondary infection, 44 Gm. of sulfanilamide was given from August 12 to August 22 inclusive without effect. The drug was again given from October 14 to October 17 inclusive, 16 Gm. being administered. The other medications given during this period were tannic acid, silver nitrate, boric acid ointment, potassium permanganate and dilute solution of sodium hypochlorite locally, and morphine, codeine, phenobarbital, acetophenetidin, acetylsalicylic acid and chloral derivatives. The Kline test for syphilis was negative.

November 30 a generalized erythematous maculopapular eruption appeared. Within the next week this progressed into an exfoliative dermatitis. The patient also became icteric and the edge of the liver, previously not palpable, was now 6 cm. below the costal margin. The icteric index rose rapidly to 115 and large amounts of bile appeared in the urine. There was no concomitant anemia. December 22 the skin started to improve and returned to normal rather rapidly. The icterus decreased slowly, as did the size of the liver. Feb. 4, 1938, when he was discharged, the icteric index was 20, the liver was no longer palpable and the patient felt normal.

#### COMMENT

In case 1 there is no reasonable doubt that sulfanilamide caused the dermatitis and hepatitis. No other medication was administered, and the cutaneous eruption was a typical dermatitis medicamentosa, the hepatic disease a typical toxic hepatitis.

The case is extraordinary in that there was simultaneous occurrence of jaundice and ascites with recovery. The first description of a case of jaundice and ascites with recovery is accredited to Jones and Minot<sup>5</sup> in 1923. Subsequently similar observations have been made by Bauer,<sup>6</sup> Weir,<sup>7</sup> Meyer and Learner,<sup>8</sup> McCabe and Hart,<sup>9</sup> Cavanagh,<sup>10</sup> Pavel and Runcan,<sup>11</sup> Forbes<sup>12</sup>

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and Boros.<sup>13</sup> These reports have indicated that arsenamine, mercurial products, phosphorus, sodium gold thiosulfate, cinchophen, common duct stone, pressure of glands on the common duct and infections are agents which can so damage the parenchyma of the liver as to produce both jaundice and ascites and yet permit recovery. Evidently sulfanilamide can be added to this list.

In case 2 there seems to be little doubt that the dermatitis and hepatitis were caused by sulfanilamide. No other medication had been administered and the dermatitis and hepatitis in general resembled those in case 1. Either the patient had a chronic secondary anemia or the drug was hemolytic to erythrocytes. However, the size of the liver and the degree of icterus would indicate that an acute inflammatory process was present in any event and that the jaundice was not a manifestation of hemolytic anemia. Death in this case cannot be ascribed to the hepatitis alone in view of the fact that exfoliative dermatitis and anemia were also present.

Case 3 illustrates a less severe degree of hepatitis, occurring in this instance in a patient addicted to alcohol. No medication other than sulfanilamide was administered. Whether previous ingestion of alcohol renders the liver more vulnerable to sulfanilamide cannot be stated, although numerous other patients who have used alcohol to excess have tolerated the drug satisfactorily.

Case 4 reports a typical case of toxic hepatitis of moderate severity. No etiologic agent other than sulfanilamide can be incriminated. In this case, as in case 3, there were no other toxic manifestations.

The hepatitis in case 5 cannot be ascribed to sulfanilamide with as much certainty as in the other cases. In this instance there had been an interval of forty-three days between the last dose of sulfanilamide and the onset of symptoms. However, during this period no drug ordinarily considered as capable of causing toxic hepatitis and dermatitis had been administered. Furthermore, in the case of other hepatic irritants the length of time intervening between the actual administration of the drug and the onset of symptoms has been found to be quite variable, occasionally being as much as several months.<sup>14</sup> Whether this will hold true for sulfanilamide as it has in the case of other drugs remains to be seen. Certain it is that the hepatitis and dermatitis in this case were virtually indistinguishable from those in case 1 and case 2.

SUMMARY

Four cases of toxic hepatitis occurred during the course of sulfanilamide therapy. No other medication had been given to these patients. A fifth case developed after the use of sulfanilamide had been discontinued. In this instance the patient had received other medications but none ordinarily considered as capable of causing toxic hepatitis.

Three of these cases of toxic hepatitis showed an associated exfoliative dermatitis and one ended fatally. One case was extraordinary in that there was a simultaneous occurrence of jaundice and ascites with recovery.

This experience indicates that sulfanilamide should be added to the list of agents which may cause severe damage to the liver.

3395 Scranton Road.

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RADIOACTIVE IRON AND ITS METABOLISM IN ANEMIA

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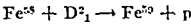
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During the past eight months radioactive iron has been used in these laboratories as a tool in the studies of iron metabolism in dogs. This radioactive iron is prepared from the  $\text{Fe}^{58}$  isotope by deuteron bombardment



Its beta ray activity with a half life of forty-seven days makes this isotope useful as a labeled iron that may be followed in metabolism experiments even after mixture with the ordinary iron in the body.

Physiologists will admit that our understanding of iron metabolism is in a parlous state. There are diametrically opposed views relating to almost every phase of iron metabolism in the body. It is fair to state that much of this difficulty relates to methods of iron analysis. Many methods for iron analysis in body tis-

Radioactive Iron Content of Tissues and Blood: Percentage of Total Amount Fed

	Anemic				Normal			
Dog.....	H-9	H-8	37-116	37-227	37-77	37-141	37-214	
Hours after last feeding?.....	20	23	23	4	75	84	23	7
Liver.....	0.4	0.4	0.5	..	..	0.2	0.03	0.02
Spleen.....	0	0	0.1	..	..	0	0.02	0.005
Marrow.....	0.2±	3±	2±	..	..	0	0.03±	....
Plasma.....	0	0.3	0.11	0.7	0	0	0.017	....
Red blood cells.....	8.7	9.0	1.4	0.9	4.6	0.04	0.06	....
Whole blood.....	(8.7)	(9.3)	(1.5)	(1.6)	(4.6)	(0.04)	(0.07)	0.05
Total absorbed	9.3	12.7	4.1			0.24	0.15	0.08

\* Dogs 37-227 and 37-214 were fed iron as ferric chloride; all others as ferric sulfate.

sues, fluids or feces carry errors so large as to render the results useless. These errors are due in part to various compounds of calcium and phosphorus.

If one may state (with allowance for varied opinions) the generally accepted story of the absorption and excretion of iron, it would read as follows: Iron is absorbed from the upper part of the intestinal tract in amounts depending on its concentration in the food, its form (ferrous or ferric) and gastric acidity; the surplus related to iron absorption, utilization and wastage is excreted in the lower bowel.

It came as a great surprise to us that iron is absorbed only in traces by a nonanemic dog but in abundance by the anemic dog depleted of its iron. This point is clear from a review of the accompanying table, but we are not prepared to say on what factors this difference rests—whether changes in mucosa, plasma or concentration of organic iron are of primary importance.

Five dogs were maintained on a diet low in iron and kept anemic by frequent bleeding. This has been shown to affect the depletion of iron stores. They were then fed iron containing the radioactive isotope on one or several occasions and the absorption of iron was followed by analysis of the circulating blood fractions. In three experiments the dogs were killed with ether after careful viviparfusion to remove all the circulating blood

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from the viscera. The value and limitations of this technical procedure have been discussed.<sup>1</sup> The content of radioactive iron in the liver, spleen and marrow was then determined, as shown in the table.

In another series of experiments, radioactive iron was fed to three normal dogs with iron stores well filled as the result of previous feeding of soluble iron salts and intravenous injections of neutral colloidal iron.

It is immediately apparent, even in this short series, that the nonanemic animal absorbs but little of the iron fed. Some of the anemic animals were not perfused in order that studies of excretion over long periods of time might be made, so we have no values for the iron content of the viscera. However, the rapid appearance of the isotope in the plasma and red blood cells alone is in marked contrast to the evidence in all the viscera and blood of the normal animals examined. The rapid appearance of radioactive iron in the red blood cells is of great interest. A discussion of the significance of these observations must await further experiments to indicate the relationship of this iron to the hemoglobin of the various types of red blood cells (nucleated, immatur and mature).

#### CONCLUSION

The evidence appears convincing that, in dogs under the conditions of these experiments, absorption of iron is dependent on the need of the body for iron.

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### A REACTION TO THE ORAL ADMINISTRATION OF NICOTINIC ACID

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Almost all the reports on the treatment of pellagra with nicotinic acid refer to unpleasant, but harmless, reactions. Fouts, Helmer, Lepkovsky and Jukes<sup>1</sup> treated three cases of pellagra with 500 mg. and one case with 1 Gm. of nicotinic acid. A sensation of heat and tingling on the skin was noted in all four cases. These sensations appeared within ten minutes, lasted from ten to twenty minutes, and were accompanied by dilatation of the peripheral blood vessels and slight, temporary fall in blood pressure.

The Smiths and Ruffin<sup>2</sup> observed a marked flushing of the face, neck, chest and arms a few minutes after intramuscular injection of 60 mg. of nicotinic acid, which lasted for fifteen minutes. A similar reaction followed the intravenous administration of approximately 12 mg. They note that the pulse, respiration and blood pressure were not affected and that there was no discomfort except for a slight feeling of warmth.

Spies, Cooper and Blankenhorn<sup>3</sup> noted severe flushing, itching and tingling, particularly of the face and

extremities, within twenty minutes after the administration of nicotinic acid in nine of thirteen persons. At the peak of the flushing there was no effect on blood pressure, temperature or respiration, and they state that in no instance did the administration of less than 50 mg. produce any effect, the reaction usually occurring only when large amounts were given.

France, Bates, Barker and Matthews<sup>4</sup> report mild generalized sensations of tingling and flushing in a case of pellagra a few minutes after the intramuscular injection of 60 mg. of nicotinic acid.

Spies, Bean and Stone<sup>5</sup> found that oral doses of 200 mg. of nicotinic acid or intravenous doses of 10 mg. nearly always produce a reaction within one minute. They noted reactions in about 5 per cent of 100 adults with an oral dose of 50 mg. and in about 50 per cent when 100 mg. was given. The reaction was characterized by flushing, burning and itching sensations with increased temperature of the skin and increased gastrointestinal motility. The pulse, blood pressure, respiration and electrocardiograms were not regularly changed.

Ruffin<sup>6</sup> states that 1 Gm. daily given in four doses invariably produces unpleasant sensations and flushing of the face and neck. In two of ten cases nausea and vomiting occurred.

Bogart<sup>7</sup> gave one patient 500 mg. daily until 8 Gm. was given and 300 mg. daily until 6 Gm. was given, and noted redness and warmth of the skin on only two occasions.

Rachmilewitz and Glueck<sup>8</sup> report one case of pellagra with tingling of finger tips, flushing of face and dizziness following 250 mg. of nicotinic acid for one day and 350 mg. daily for four days. In a second case severe itching occurred over the dermatitis, with flushing of the face, faintness and urticarial rash over the knees, back and arms following a second dose of 50 mg.

In view of these reports it seemed desirable to determine the quantity of nicotinic acid which may be given by mouth to healthy subjects without producing these unpleasant reactions which tend to make continued treatment with the drug more difficult. Accordingly, a group of eighteen healthy adult women were given an identical diet containing approximately 2,400 calories and low in the pellagra-preventive vitamin. Six were given 50 mg., six 30 mg. and six 10 mg. of nicotinic acid daily in aqueous solution added to 4 ounces (120 cc.) of tomato juice and taken with the mid-day meal. On the twelfth day of administration one of the subjects receiving 50 mg. daily (total intake of nicotinic acid 600 mg.) showed an intense flushing of the face, chest and back, accompanied by mild itching and a sensation of heat in the skin, which appeared in from ten to fifteen minutes after administration of the nicotinic acid and disappeared after about an hour. Following this first reaction, each daily dose of 50 mg. produced a similar reaction for eleven days. The dose was then divided into 25 mg. morning and evening. The flushing became much less marked and the subjective symptoms were milder but still occurred.

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On the sixteenth day of administration a second subject receiving 50 mg. daily (total intake of nicotinic acid 800 mg.) showed a similar reaction of severe flushing of the face.

On the twenty-seventh day two more of the group receiving 50 mg. of nicotinic acid daily (total intake of nicotinic acid 1,350 mg.) showed similar reactions of slight flushing, itching and a sensation of heat. The remaining two subjects of this group did not show any reaction during a period of ninety-two days on the 50 mg. of nicotinic acid daily.

One of the six subjects receiving 30 mg. of nicotinic acid daily had a reaction on the thirty-second day (total nicotinic acid 660 mg.), characterized by an intense flushing of the face and neck, with itching and a sensation of heat. When the dose was continued the reaction occurred occasionally.

On the ninety-second day a second subject receiving 30 mg. daily (total intake of nicotinic acid 2.76 Gm.) had a similar reaction, which was unusual in that the flushing was restricted to the skin of the forehead, bridge of the nose, cheeks, back of the neck, shoulder joints, elbows, buttocks and knees. The remaining four subjects in the group did not show any reaction during the period of ninety-two days on the 30 mg. of nicotinic acid daily. None of the six subjects receiving the 10 mg. dose of nicotinic acid had a reaction at any time during the ninety-two days of observation.

The four subjects in the 50 mg. group who had reactions weighed 128, 101, 140 and 108 pounds (58, 46, 63.5 and 49 Kg.). The two who had no reactions weighed 165 and 111 pounds (75 and 50 Kg.). The two subjects in the 30 mg. group who had reactions weighed 119 and 113 pounds (54 and 51 Kg.). The remaining four weighed 147, 132, 99 and 143 pounds (67, 60, 45 and 65 Kg.). Thus there appears to be a considerable individual variation in reactions to nicotinic acid given by mouth which does not depend on the relationship between dosage and body weight, although this cannot be stated with certainty since the degree of saturation of the subjects with nicotinic acid at the beginning of the test is unknown.

In view of the fact that the reactions did not recur regularly in any of the patients except one in the 50 mg. group, and since Spies, Bean and Stone<sup>5</sup> report reactions within one minute from the intravenous injection of 10 mg., and the Smiths and Ruffin<sup>2</sup> report reactions from 12 mg. intravenously, it is not unlikely that one of the controlling factors in this reaction to the oral administration of nicotinic acid is the rate of absorption from the gastrointestinal tract.

#### CONCLUSIONS

Nicotinic acid in daily doses of 50 mg., given orally, produced transient, unpleasant but harmless reactions in four of six adult women on a diet restricted in the pellagra-preventive factor. A daily dose of 30 mg. of nicotinic acid produced a similar reaction in two of six women. Therefore reactions are to be expected in some persons on continued treatment with nicotinic acid in daily doses as low as 30 mg. by mouth.

Although the reactions are disagreeable, they persist only a short while and there is no evidence that any harm is done by them. Therefore their occurrence should not be allowed to interfere with the therapeutic use of large doses of nicotinic acid.

## THE PRIVATE PHYSICIAN'S ROLE IN THE NEW YORK CITY SYPHILIS CONTROL ACTIVITIES

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Not merely in words but also in action the New York City Department of Health has expressed its belief that the role of the private physician in the control of syphilis and gonorrhea is of paramount importance. There are about 15,000 private physicians in this city. They are in every neighborhood, available to aid diseased persons with advice, diagnosis and treatment. A large percentage of them welcome the opportunity to give medical care to persons having syphilis or gonorrhea and they welcome that official aid which enables them to render these services to a larger and larger number of victims of infection. They are willing to learn modern methods of diagnosis and treatment if they are not already familiar with them. They are willing to use modern diagnostic facilities, to seek consultation, to accept appropriate drugs, to report their cases, to cooperate in finding sources of infection, to notify the department of health regarding lapsed cases and to aid in popular education of the general public regarding syphilis and gonorrhea. They benefit and the official health agency benefits by this cooperation.

The health department should study seriously and frequently the question What can we do to help private physicians find, treat and keep under treatment more and more persons with gonorrhea and syphilis, especially those who can pay a fee, even though a very modest one? No health department can afford to neglect measures for obtaining the cooperation of private physicians. If the cooperation of the official agency is sincere—with emphasis on the "co"—and not merely a onesided demand for reports and red tape performances from private physicians, the results will be satisfactory to all concerned.

Cooperation with private physicians was the basis of the policy of the New York City Department of Health when in October 1935 Commissioner John L. Rice created a Bureau of Social Hygiene to develop a program for the control of syphilis and gonorrhea in our population of seven and a half million people. Administrative details have been carefully considered with the medical advisory committees of the department and of the several health districts of the city.

As a preliminary step in this process of cooperation with private physicians a twofold plan of disseminating popular and professional information was set up. In order to meet the needs of practitioners who were not thoroughly familiar with modern methods of diagnosis and treatment of syphilis and gonorrhea, four post-graduate clinical courses, each of six weeks' duration and requiring attendance three times weekly, were given in succession in 1937. Registration was limited to ten physicians for each of these sessions, which included lectures and clinical demonstration. During the spring of 1938 a "refresher course" was held once a week for six weeks; the attendance throughout was maintained at seventy doctors for each meeting. In fact, this course was so well received that it was



decided to hold a similar series during the summer months. In spite of the seasonal inactivity, an average of forty physicians attended each session. Local and national medical groups holding periodic meetings in New York City include in their programs sections on control of syphilis and gonorrhea. For example, during the week of the annual meeting of the American College of Physicians, one section met daily at the

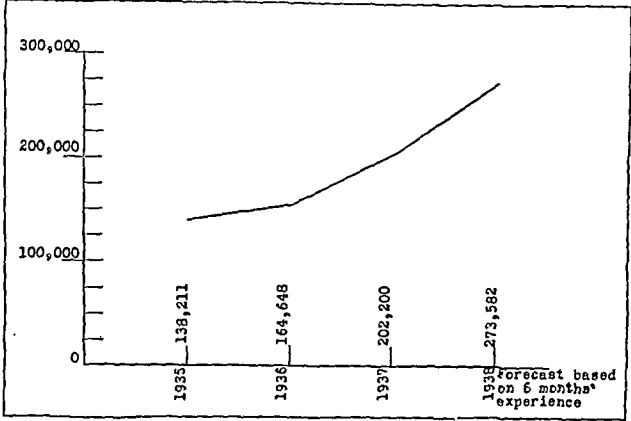


Chart 1.—Specimens tested for private physicians, health department laboratory, 1935-1938.

department of health for lectures, discussion and clinical demonstration on problems of research in and diagnosis and treatment of these diseases. The Academy of Medicine sponsored a series of lectures on syphilis and gonorrhea in 1937. In addition to these educational activities, informative literature is distributed by the department of health for professional use. In 1936, 1,400 physicians in the city received a practical pamphlet on syphilis, and during the first half of 1938, 2,107 pamphlets entitled "Syphilis—Its Diagnosis and Treatment" were sent to local practitioners.

Private practitioners have in turn united with the health department in enlightening the general public. During the 1937-1938 season, forty-five doctors, not connected with the department in any way, gave eighty-one lectures, accompanied by film showings, to general

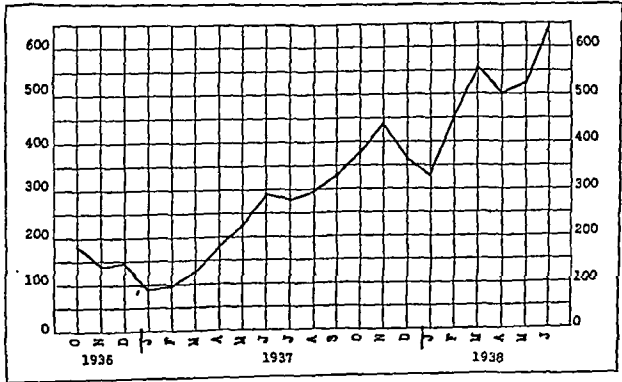


Chart 2.—Number of private physicians receiving drugs, October 1936 to June 1938.

lay audiences. These doctors are included in a panel of speakers and generously volunteer their own time, without remuneration, to cooperate in the popular educational program. Thousands of physicians participate by distributing large quantities of literature, consisting of simple explanations of facts about syphilis and gonorrhea prepared in various languages for different population groups.

All educational propaganda issue by the department of health stresses the desirability of undergoing examination and treatment, if necessary, by the family physician. Every possible aid is extended to the doctor in carrying out this objective. Among diagnostic services offered the physician is free laboratory service, including blood, dark field and spinal fluid examinations for syphilis and smear tests for gonorrhea. One-half million such tests are performed annually in the health department laboratories, and of these more than 50 per cent are sent in by private physicians. That this service is constantly increasing is evident by chart 1.

Private physicians may send their patients to any one of twenty centers for diagnostic and consultation services; the results of such examinations, which vary from the taking of a specimen to performing a complete examination for a venereal disease, are sent directly to the physician referring the patient. Table 1 indicates the number of laboratory specimens taken in health department clinics on patients referred by private physicians; it will be noted that an increase of 20 per cent over the number examined in 1937 is expected in this service during 1938.

The department of health has repeatedly announced that persons wishing to place themselves under the care of private physicians can obtain the names of private physicians from the diagnostic and treatment centers of

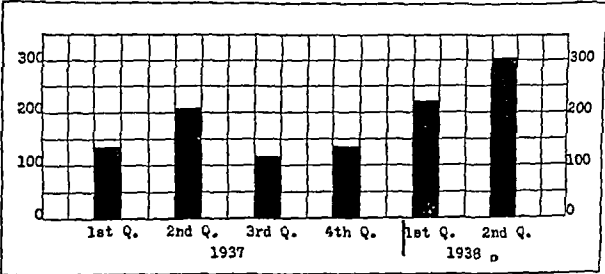


Chart 3.—Private physicians visited by epidemiologists, 1937-1938.

the department. The five county medical societies of New York City have supplied the department with names of doctors qualified and willing to receive patients referred by the department for diagnosis and treatment of syphilis and gonorrhea at moderate fees. Five of these names, selected in strict rotation, are given to each applicant for private medical care, who makes his own final selection of a doctor. Since this system was begun early in 1937, more than 600 persons have been so referred.

However, when a patient cannot afford even these substandard rates for diagnostic services, he is examined and later referred to a private physician for treatment if necessary and if his economic status permits. From 200 to 300 persons annually are referred to private physicians for treatment subsequent to examination in health department clinics. A reciprocal relationship allows the private doctor to send his patients to the health department for treatment if he finds such an arrangement desirable; more than 1,000 patients are referred by private physicians each year for treatment by the department of health.

One of the most important items in placing and keeping patients under the care of private physicians is the practice of the distribution of free drugs for the treatment of syphilis. From August 1936, when distribution began, through June 1938, a period of twenty-two months, 420,448 doses of drugs were given

to private practitioners for the treatment of their private patients, regardless of their economic status and in sufficient amounts to give thorough and complete treatment. More than 600 doctors a month receive drugs for the treatment of almost 1,000 patients. Chart 2 indicates the extent to which this practice is expanding.

The problems of helping physicians to find new patients with syphilis and gonorrhea and keep them under their care have been satisfactorily solved by the methods briefly outlined. However, the necessity for extending these services to provide for the investigation of contacts, sources of infection and the follow-up of delinquent cases was met by employing, in December 1936, a staff of four medical epidemiologists and eight nurse epidemiologists. Any physician is at liberty to request the assistance of a member of this group, who, for the duration of his relationship with the physician, serves under the latter's supervision.

Medical epidemiologists, on request, frequently confer with doctors regarding their problems of diagnosis and treatment and help them bring in for examination possible sources of infection and contact to their patients. Chart 3 indicates the number of visits made to private physicians by epidemiologists, at the physicians' request.

During 1937, 433 named possible sources of infection were referred by doctors for investigation, of whom

TABLE 1.—Specimens Taken for Private Physicians at Social Hygiene Clinics for Wassermann, Dark Field and Smear Examinations in New York City, 1935-1938

1935	1936	1937	Forecast for 1938*
13,006	11,554	12,815	15,172

\* Based on six months' experience.

TABLE 2.—Reported Cases of Syphilis and Gonorrhea in New York City During First and Second Quarter of 1938

Reporting Agency	First Quarter	Second Quarter	Percentage Increase
State Department of Health	1,506	3,542	135
City Department of Health	4,149	5,489	32
Private Physicians	2,593	5,857	126
Other	35	1	-97
Totals	8,283	14,889	80

134, or 31 per cent, were subsequently proved sources of infection. They also referred 217 contacts to their patients, of whom 204, or 94 per cent, were brought in for examination. Thus, it is obvious that one of the major obligations of the medical epidemiologist is serving the private practitioner in any capacity relevant to the control of syphilis and gonorrhea.

Nurse epidemiologists follow up patients reported as delinquent by private physicians; in their dealings with these patients they act as agents of the doctors. Their chief concern is the return of the patient to the referring physician; if such action is impossible, the nurse makes an effort to place him under other medical supervision. During the second quarter of 1938 a brief study was made of the results of following up and tracing delinquent patients reported by private practitioners. In this period 360 new referrals were made, of which 270 were terminated. Of these 270 terminations, 103 were not found because the patient had given the physician a false address or because the patient had left the city. Thus 167 of these persons were located, of whom 50 per cent were returned to private physicians. Most doctors are not able to follow up their own delinquent patients and find it very convenient to enlist the help

of a nurse epidemiologist. As more doctors become familiar with this service, more of the nurses' time is devoted to their patients. Chart 4 shows the ratio of private physicians' cases to the total number of lapsed cases referred for follow up since the beginning of 1937, when this item in the control program was introduced.

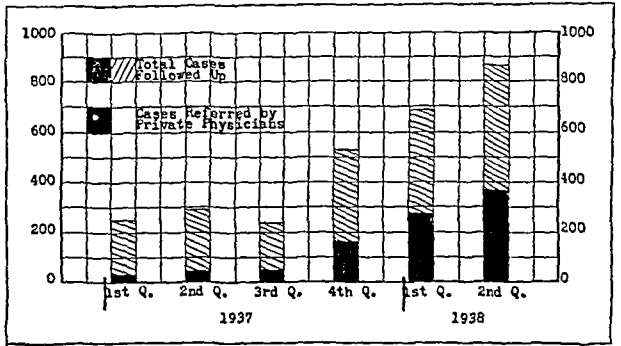


Chart 4.—Cases referred by private physicians for follow up by nurse epidemiologists.

Case reporting by private physicians has improved to the extent at which it is now possible to omit positive laboratory reports from the official case count. Every physician who submits to the health department laboratories a positive blood or smear specimen is sent a letter requesting him to report the patient if a diagnosis of syphilis or gonorrhea is made and if the report had not previously been made. These individual letters

NEW YORK CITY DEPARTMENT OF HEALTH  
BUREAU OF SOCIAL HYGIENE

Facilities available without cost to Physicians in Practice  
For Complete Information—Phone WOrth 2-6900  
Extensions 214-215-252

1. Laboratory Examination:  
(a) Dark field for *Spirochaeta pallida*.  
(b) Smears for gonococci and Ducey bacilli.  
(c) Blood Wassermann tests.  
(d) Spinal fluid examination for neurosyphilis.  
(e) Frei tests for lymphogranuloma venereum.

2. Lumbar Puncture.

3. Clinical Consultation Service (Diagnosis and Treatment).  
Reports mailed only to referring physician.

4. Antisyphilitic drugs: Neoarsphenamine and bismuth compounds distributed free of charge.

5. Epidemiologic Service:  
As representative of referring physician.  
(a) Investigation of sources of infection on request and only with consent of physician.  
(b) Follow up of family and other contacts and cases lapsing treatment.

6. Postgraduate instruction in the diagnosis and management of syphilis.

7. Clinical conferences at the Bureau of Social Hygiene.

8. Posters and literature for patients.

9. Listing through local county medical society qualified physicians willing to treat referred patients at moderate fees.

Preserve This Card for Future Reference

Announcement sent by laboratory with reports on specimens.

are not only directly responsible for the great improvement in case reporting but have also proved to be a valuable means for bringing to the attention of the department delinquency in treatment. This system was instituted during the first quarter of 1938 and has begun to produce excellent results. During the first three months of the year 8,281 cases of syphilis and gonor-

rhea were reported as compared with 14,889 for the second quarter, an increase of 80 per cent. It is particularly interesting to note that private physicians have improved their official case reporting during that time by 126 per cent and now constitute the largest reporting agency, as indicated in table 2.

The greatest problem still remaining in this program of coordinating the activities of the medical and public health professions is that of acquainting more doctors with the services offered them. In their efforts to inform their members of health department activities in this connection, the local medical societies have published progress reports and occasional editorials in their official bulletins. The department of health has repeatedly circularized the profession by means of general letters, through the press and by personal contact as well as through the laboratory, which sends announcements (such as the card reproduced herewith) in a routine manner with reports on specimens. The demand for services is rapidly increasing as a result of this publicity; the department will continue to keep pace with this growing interest by emphasizing cooperation with the medical profession.

#### SUMMARY AND CONCLUSION

In New York City the department of health offers to private physicians postgraduate educational opportunities, all diagnostic and consultation services, epidemiologic and follow-up services, and drugs for the control of syphilis and gonorrhea. The private practitioners of the city have welcomed these services and have given their cooperation in finding and treating these diseases.

50 West Fiftieth Street.

## Clinical Notes, Suggestions and New Instruments

### SENSITIZATION REACTION TO SULFANILAMIDE

E. B. ROGERS, M.D., EL PASO, TEXAS

Many reports of eruptions of the skin have been described as having resulted from sulfanilamide. Dermatitis medicamentosa, a simple maculopapular rash, has appeared during the second week of treatment in about 6 per cent of cases.<sup>1</sup> It usually disappears in two or three days after treatment has been discontinued. Erythematous eruptions covering part or all of the body have been described<sup>2</sup> and there have been some cases of exfoliative dermatitis which cleared up only after several months.<sup>3</sup> Only one report of definite sensitization to the drug has come to my attention, in an unpublished personal communication; hence the following case report seems worthy of notice.

#### REPORT OF CASE

Mrs. R., aged 58, an American housewife with two children, gave a past history of allergy. In 1921, to relieve severe pruritus vulvae, a resection of the left ilio-hypogastric and ilio-inguinal nerves was done under 1 per cent procaine hydrochloride local anesthesia. Later a tooth was extracted with procaine hydrochloride as the anesthetic agent. No reaction resulted. In 1923 a sebaceous cyst was removed from the back of the neck under procaine hydrochloride. After about a week an area of redness appeared in the surrounding skin which had the appear-

ance of an infection, but there was no pus at any time. There was much itching, which disappeared together with the redness in about three weeks. Three years later another dentist blocked a nerve with tutocain, assuring her that this was not procaine hydrochloride and would not produce a reaction. However, a severe reaction followed with redness and swelling. The gums healed slowly over a period of three or four weeks. At another time the addition of butyn to a prescription for pain in the left eye caused redness, itching and closure of the eye from swelling within twenty-four hours. The reaction was severe for a week and cleared up in three weeks. In 1930 a thoracentesis was done by one of my associates, who used procaine hydrochloride, not knowing the patient was allergic to this anesthetic. Resection of a rib was then done under gas. The area about the wound became red after a few days but the patient was too ill with empyema to note subjective symptoms.

In 1935 the patient had erysipelas originating in a small area of eczema above the right ear, which yielded to treatment with ultraviolet rays. Early in May 1938 a threatened return of the erysipelas led to sulfanilamide therapy. She took five tablets, a total of 25 grains (1.6 Gm.) in thirty-six hours. The next morning her left eye was red and the lids were greatly swollen. The conjunctiva was much congested and there was marked lacrimation. Bright red erythema covered the lids and spread over about 1 inch (2.5 cm.) of the surrounding skin. Itching of the lids was intense, especially along the margins and at the outer canthus. The right eye was normal. At the same time an area of erythema and swelling appeared in the left groin, centering over the site of the resection of the nerves, and extended gradually for a period of about two weeks. The swelling extended about 3 inches (7.6 cm.) in advance of the erythema and was marked by a sharply defined raised border similar to erysipelas, but the tissues were very soft. The temperature and pulse were normal throughout.

In the succeeding three to ten days every site of a previous application of a local anesthetic flared up in reaction—bright red erythema, itching, swelling and tenderness on pressure. The site of injection on the neck flared up on the third day, the site of injection for resection of the rib on the sixth day and the buccal mucosa about the tenth day, and later the eczematous area was found to present a red rash. The time of appearance and the intensity of reaction in all three areas seemed to depend on the quantity of anesthetic that the tissues had received at the time of operation. The eye, commonly used for sensitization tests, reacted first, and no one could fail to see that the ophthalmic reaction was strongly positive. The reaction on the groin spread over the abdomen and both thighs. The erythema in the neck and chest reached diameters of 6 and 10 inches (15 and 25 cm.). The reaction in the patch of eczema was small; it probably resulted from an external application of an anesthetic ointment. The reaction of the buccal mucosa was limited to the mucous membrane of the mouth, tongue and throat. The process in all the affected areas reached its height during the third week, at which time fully one third of the body surface was involved. Decline of the reactions then began very slowly, and at the end of five weeks there is still itching and erythema in the groin and on the back. She is not allergic to proteins, unless the eczema is of that nature.

An intolerable itching in all the affected areas was the principal symptom. Neither epinephrine nor ephedrine had any effect. The best relief was obtained from antipruritic lotions containing phenol or from the soothing effect of starch water. At one time the patient applied ethylaminobenzoate (anesthesin) ointment over a small area, which gave temporary relief but later aggravated the symptoms. Barbiturates were necessary for sleep.

The chemical formulas are given here for comparison:

Procaine hydrochloride—para-amidobenzoyl diethylaminoethanol hydrochloride.

Tutocain—para-aminobenzoyl dimethylaminomethyl-butanol hydrochloride.

Butyn—para-aminobenzoyl gamma-di normal butylaminopropanol sulfate.

Sulfanilamide—para-aminobenzene sulfonamide.

Anesthesin—ethyl aminobenzoate.

1. Schwentker, F. F., and Gelman, Sidney: Bull. Johns Hopkins Hosp. 61: 136 (Aug.) 1937.

2. Finney, J. O.: Severe Dermatitis Medicamentosa Following the Administration of Sulfanilamide, J. A. M. A. 109: 1982 (Dec. 11) 1937.

3. Myers, G. B.; Vonder Heide, E. C., and Balcerski, Matthew: Exfoliative Dermatitis Following Sulfanilamide, J. A. M. A. 109: 1983 (Dec. 11) 1937.

The base of each of these compounds is aminobenzene (aniline). From the injections of procaine hydrochloride the patient evidently became sensitized to compounds containing this base. If the sulfanilamide had been given by injection the result would doubtless have been the same—a flare-up reaction in areas that had previously been sensitized. Cutaneous scratch tests gave a positive wheal to 2 per cent procaine hydrochloride in twelve hours, redness in twenty-four hours, followed by itching and swelling in the subcutaneous tissues which increased gradually for a week before recession began. There was a slight reaction to aminobenzene, none to sulfanilamide. Patch tests gave negative results. Eight days after the patch tests were applied the 2 per cent procaine test gave a positive result with a papulovesicular (2 cm. in diameter) rash that faded out slowly, about two weeks later. The notable feature is that a drug taken by mouth should produce reactions at the sites of injections made years before and at no other place. This would seem to mark the process as a form of allergy but differs from food allergy in that the reaction occurs only in areas previously sensitized by some derivative of the aminobenzene base.

610 Martin Building.

# STANDARDS FOR RED BLOOD CELL INCREASE AFTER LIVER AND STOMACH THERAPY IN PERNICIOUS ANEMIA

RAFAEL ISAACS, M.D.; FRANK H. BETHELL, M.D.; MATTHEW C. RIDDLE, M.D., AND ARNOLD FRIEDMAN, ANN ARBOR, MICH.

Data from 129 selected patients with pernicious anemia in relapse, adequately treated with liver extract intramuscularly, and twenty-one patients treated with desiccated, defatted stomach tissue have been analyzed to note the rate of increase in the red blood cell count. The dosage of liver extract averaged the

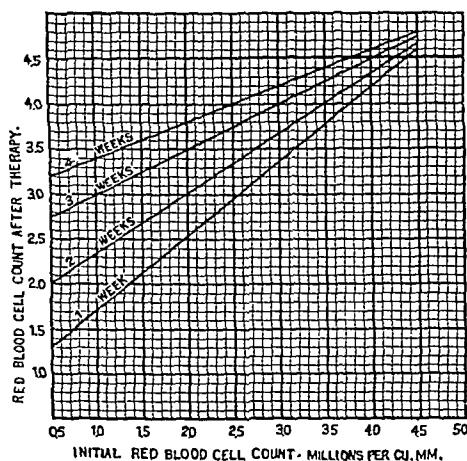


Chart 1.—The red blood cell count after one, two, three and four weeks of intramuscular liver extract therapy. Example: With an initial red blood cell count of 2 million per cubic millimeter the count at the end of one week will be 2.55 million, at two weeks 3 million, at three weeks 3.5 million, at four weeks 3.8 million.

equivalent of from 1 to 2 units daily, and the desiccated stomach dosage was usually 40 Gm. daily for the first two weeks.

In chart 1 the red blood cell count at the beginning of intramuscular liver extract therapy is plotted against the red blood cell count at the end of one, two, three and four weeks. A separate line is drawn for each week. The lines have been smoothed and corrections have been made for deviations due to manifest abnormalities and inadequate data at various points, as indicated by evident interpolations. Data from more than 500 cases were available for such changes.

In chart 2 the same data are plotted, showing the average rate of formation of red blood cells after intramuscular liver extract therapy, in terms of weekly changes for each initial count. From the trend of these lines, checked by available

From the Thomas Henry Simpson Memorial Institute for Medical Research, University of Michigan.

data, the positions for five, six, seven and eight weeks are indicated. If the rate remains unchanged a count of five million red blood cells per cubic millimeter may be expected at the end of eight weeks, regardless of the initial count. Many factors may modify this in individual cases, such as infection, deficiency of iron and an abnormal rate of blood destruction.

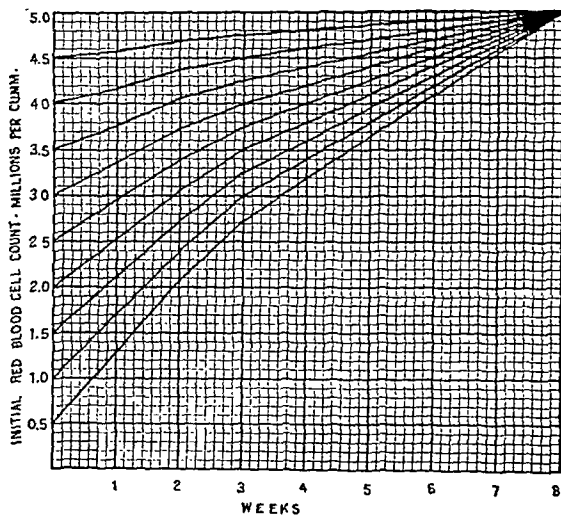


Chart 2.—The red blood cell count, at weekly intervals, for each initial red blood cell count after liver extract therapy, intramuscularly. Example: With an initial red blood cell count of 1 million per cubic millimeter the count at the end of one week will be 1.7 million, at two weeks 2.4 million, at fifteen days 2.5 million, and so on.

The rate of increase of red blood cells is slower during the first two weeks after desiccated defatted stomach tissue is given than after intramuscular liver extract (chart 3). An analysis of these data, if plotted with "weeks" as ordinates and the "initial red blood cell count" as abscissas, shows that the rise in the red blood cell count, after stomach medication, is very slight during the first week, contrasting with the more rapid increase after intramuscular liver extract medication. It is pos-

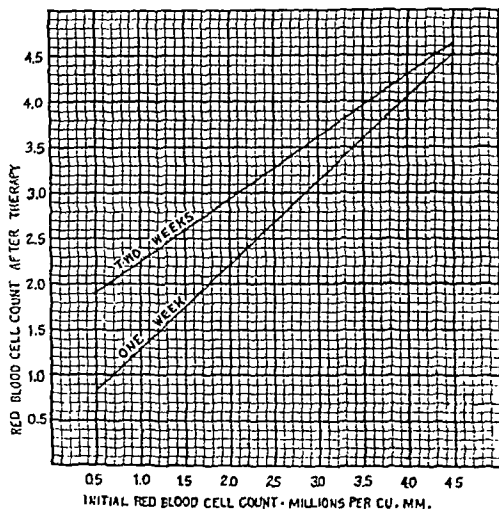


Chart 3.—The red blood cell count after one and two weeks of therapy with desiccated, defatted stomach tissue. (See example in legend for chart 1.)

sible that this is related to the speed of absorption of the material by the intramuscular route. The slope of the line shows that the rise would begin on the fourth day of treatment with stomach.

## SUMMARY

Standards are given for the red blood cell counts, at weekly intervals, for patients with pernicious anemia treated with liver extract intramuscularly and for desiccated defatted stomach therapy.

## QUININE IN MYOTONIA CONGENITA

ROBERT B. LONERGAN, M.D., AND HARRY A. PASKIND, M.D., CHICAGO

In 1936 Wolf<sup>1</sup> reported startling effects of quinine in states of myotonia. He treated three siblings with myotonia congenita and one patient with myotonia atrophica with quinine and found that all myotonic manifestations disappeared. He reported that 10 grains (0.65 Gm.) of quinine dihydrochloride injected intravenously abolished every myotonic phenomenon within ten minutes after administration, the effect lasting from fifteen to twenty hours. He further found that quinine hydrochloride from 5 to 10 grains (0.32 to 0.65 Gm.) given by mouth two or three times a day proved to be an adequate maintenance dose for the eradication of the myotonia.

Wolf tried the remedies previously used in such states, such as thyroid substance, atropine, posterior pituitary, calcium chloride, salicylic acid and calcium gluconate, and found them without effect on his patients. Various stimulants and depressants of the autonomic nervous system and several alkaloids he found equally ineffective.

Wolf concluded that quinine is a specific for myotonia.

Previously Lindsey and Curnen<sup>2</sup> presented evidence in favor of the view that the after-contraction of myotonia is of reflex origin and is due to the persistent discharge of hyperexcitable sensory end organs in muscle. It seemed reasonable to Wolf that quinine produced effects by diminishing this reflex action. Pharmacologically it had been known before that quinine produces a transient increase in strength in skeletal muscle, followed shortly by fatigue and weakness of contraction, that it produces vascular dilatation and is an antagonist to epinephrine, and that it depresses the vagus termination.

At the meeting of the American Neurologic Association in 1937 Wolf presented a paper in which he showed cinematographically the dramatic changes produced by quinine in one of his patients with myotonia.

In 1937 Kennedy and Wolf<sup>3</sup> reported the results of treatment with quinine in four additional patients with myotonia, three of whom had myotonia atrophica and one myotonia congenita. Again they found that quinine hydrochloride, given by mouth in doses of from 5 to 10 grains, was followed by disappearance of the myotonia. They also reported that quinine and prostigmine are antagonistic in action, quinine aggravating the symptoms of myasthenia gravis and prostigmine having the same effect in myotonia.

In discussing the pathogenesis of myotonia, Kennedy and Wolf pointed out that endocrine factors may play a part. Thus, myotonia had been observed periodically during the menses, its cessation had been observed after the birth of a child, and improvement had been noted after administration of calcium and parathyroid. As a result of experiments, Kennedy and Wolf concluded that the myotonus of myotonia congenita is a pathologic condition of the muscle or neuromuscular junction, independent of the central nervous system and, further, that quinine relieves myotonus primarily by direct action on the muscle or at the myoneural junction. They came to this conclusion after determining experimentally that spinal anesthesia does not abolish myotonia but that administration of quinine in a person previously given spinal anesthesia does abolish myotonia. They also postulated that the effectiveness of quinine in myotonia may be due to inhibition of acetylcholine production, but they felt that there were other factors at work of which there was little or no knowledge.

In another communication Kennedy and Wolf<sup>3a</sup> reported their experience with quinine in the treatment of myotonus extended over six cases of myotonia congenita and fifteen cases of myotonia atrophica for a period of one year. In not a single case did quinine fail to eradicate the myotonia. They found that any form of quinine, whether the hydrochloride sulfate,

bisulfate or hydrobromide, was effective in doses of from 2½ to 15 grains (0.15 to 1 Gm.) by mouth two or three times a day. In only one case did symptoms of cinchonism appear, as manifested by ringing in the ears.

The only other communication we have been able to find on this subject is one by Smith<sup>4</sup> in which he reported that in three cases of myotonia congenita the symptoms were entirely abolished by quinine.

## REPORT OF CASE

A youth aged 14 was first seen by us Sept. 6, 1937. The father had had two nervous breakdowns, characterized principally by depression, from both of which he recovered. The mother, the maternal grandfather and a maternal uncle all had a curious deformity of the little finger; the terminal phalanx did not lie in a straight line with the middle phalanx but instead made an obtuse angle with it. A sister, now 14 years of age, as far back as could be remembered had slight difficulty in starting to walk or run; the upper extremities were normal. We were not afforded the opportunity of studying the sister's case. The family history was otherwise negative.

The patient was the first born, born less than two years after marriage at full term. Labor was very difficult with face presentation, delivery by forceps and severe laceration. There was neither postnatal asphyxia nor convulsion. Infantile history was negative except that at first he gained weight poorly; only at the end of three months did he regain his birth weight. He had had only the ordinary diseases of childhood.

At 14 months he began to walk, and it was noted that for about one year he walked on his toes; this manner of walking then gradually disappeared. At 3 or 4 years the parents noticed that he had difficulty in starting movements, i. e. in starting to walk, in getting up from a sitting position, in climbing stairs and in starting to run. The parents were not aware of difficulty in the use of the hands, but in gross use of the arms, such as in throwing, they noticed the same difficulty in starting. All difficult movements would become easier with repetition, but hardly completely normal. Under conditions in which haste was required or under emotional strain, the disability was especially marked. This condition had been present since the onset. The disability was always worse in the morning or after a long rest but never completely gone at any part of the day, but it was alleviated considerably by exercise. There were no mental symptoms. The patient was a straight A student.

Examination disclosed the typical herculean musculature so often seen in this condition. This was especially pronounced in the quadriceps group, but the muscles of the calf, shoulder girdle, arms, back and neck also showed herculean conformation. Myotatic irritability was marked; striking with a hammer produced a furrow over any part of the skeletal muscles. The myotonic disability was easily demonstrated; there was difficulty in starting to walk, to run or to climb stairs and in squatting or getting up from a squatting or sitting position. The disability was present but less evident in the upper extremities and here was most marked in the hands and fingers; there was difficulty in grasping or shaking hands. In all affected parts the disability diminished but did not disappear after several attempts. The muscles innervated by the cranial nerves were spared; there was no difficulty with the muscles of expression, mastication, deglutition and none with the extra-ocular movements and tongue. Sensation was intact. All deep reflexes were diminished; plantar and abdominal reflexes were normal. Examination of the cranial nerves yielded negative results.

The patient had a high narrow palate, two colored irides, brown speckled with blue, and deformed fingers like those described in the mother and other members of the mother's family.

The basal metabolic rate was normal. Examination of the blood, the Kahn test on the blood and chemistry of the blood yielded negative results.

A diagnosis of myotonia congenita was made.

The patient was given quinine sulfate 5 grains three times a day. This produced improvement at once but not eradication, and increasing dosages had the same effect, i. e. amelioration only, until 10 grains was given five times a day, when disappearance of the myotonic phenomena occurred. With this

4. Smith, W. A.: Quinine Treatment of Myotonia Congenita, J. A. M. A. 108:43 (Jan. 2) 1937.

From the Departments of Orthopedic Surgery and Nervous and Mental Diseases, Northwestern University School of Medicine and the Evanston Hospital.

1. Wolf, Alexander: Quinine: An Effective Form of Treatment for Myotonia, Arch. Neurol. & Psychiat. 36: 382-383 (Aug.) 1936.

2. Lindsey, D. B., and Curnen, E. C.: An Electromyographic Study of Myotonia, Arch. Neurol. & Psychiat. 35: 253-269 (Feb.) 1935.

3. (a) Kennedy, Foster, and Wolf, Alexander: Quinine in Myotonia and Prostigmine in Myasthenia, J. A. M. A. 110:198-201 (Jan. 15) 1938; (b) Experiments with Quinine and Prostigmine in Treatment of Myotonia and Myasthenia, Arch. Neurol. & Psychiat. 37: 68-74 (Jan.) 1937.

dosage, starting to walk, run, sit up, run upstairs, shake hands and the like presented no difficulty. He was kept on this dosage for one week. After this the dosage was gradually diminished until he took one dose of 15 grains at 7 a. m. This eradicated the hypertonia until 6 p. m., and if his evening's activities required easy movements he took another 10 grains at 6 p. m.

He was last seen in August 1938. At that time he continued free from myotonic symptoms during the day if he took 15 grains of quinine sulfate in the morning, and this freedom from myotonic symptoms was continued throughout the evening if he took 10 grains more after supper.

On only two occasions were symptoms of cinchonism present in the form of ringing in the ears for short periods, and then only when he was getting 50 grains (3.2 Gm.) of quinine sulfate a day.

#### CONCLUSION

In a case of myotonia congenita we have been able to confirm the value of quinine as reported by Wolf, Kennedy and Wolf, and Smith.

25 East Washington Street.

## Special Article

### CONFERENCES ON THERAPY

#### I. TREATMENT OF PAIN

*NOTE.—These are actual reports, slightly edited, of conferences by the members of the Departments of Pharmacology and of Medicine of Cornell University Medical College and the New York Hospital. The questions and discussions involve participation by members of the college staff, students and visitors. The next report will concern "The Treatment of Coronary Disease."—ED.*

DR. McKEEN CATTELL: These conferences were inaugurated as a joint undertaking of the Departments of Medicine and of Pharmacology with the idea of stimulating interest in rational therapeutics. Representatives from the clinical departments and from the laboratory departments lead the discussion. Free and informal discussion represents the most important part of these conferences.

DR. HARRY GOLD: The symptom pain stands high, if it does not actually lead, the list of causes of disability. It is probably the most frequent symptom requiring attention in the practice of medicine. If one were to survey a fair sample of the results generally obtained with drugs for the treatment of pain, one would discover that they are not as good as they might be. The outstanding deficiencies fall into two classes:

1. First, one finds a considerable proportion of failures to abolish the pain. The primary objective seems often not to be attained.

2. Second, in a fair proportion of cases, whether the pain is controlled or not, other effects, disagreeable and sometimes disastrous, result: nausea, vomiting, constipation, distention, urinary retention, temporary blindness, deafness, skin eruptions, profuse perspiration, stupor, methemoglobinemia, agranulocytosis, acute yellow atrophy of the liver, and narcotic addiction. This is but a partial list of one that could be very much more formidable, representing the untoward reactions that follow the use of agents employed for the relief of pain.

All of this indicates that there are no ideal pain-relieving substances; our task is to consider what we need to do in order to make the drugs or medicinal agents at our disposal as effective and as safe as possible in the control of pain.

Every case of pain presents a problem. The use of drugs to control pain involves a judgment which grows out of the careful appraisal of many facts. There is a prevailing tendency in a case with pain to dig down into our bag of analgesics, fetch up something that is supposed to kill pain, and prescribe. If we do that, the range of successful treatment becomes relatively small indeed, and alongside of the little good that we do, in that way, there stands enough harm to eclipse it. Illustrations of these remarks will appear in matters that will be discussed presently.

What are the matters one needs to consider as a basis for the use of drugs in the treatment of pain, in a manner likely to yield the greatest returns with the least risk?

1. Pain is a symptom and not a disease. In our zeal to relieve it, or in our success in relieving it, there is always the danger of overlooking the less obvious and less dramatic aspect of the case, the disease itself. Recently I encountered the case of a nurse who had suffered attacks of thoracic pain. With the approval of the house officer she took large doses of an analgesic agent and obtained relief. The last attack did not respond as effectively as the previous ones, whereupon a careful examination was made. The results showed that she had been carrying on her nursing work with a pleural effusion and active pulmonary tuberculosis. This is the sort of thing one occasionally encounters. We must bear this fact in mind constantly, that pain is a symptom and not a disease, if the relief of pain is not from time to time to prove to be a misfortune.

2. Pain labels a disease and its location. This is another fact of some importance and is closely related to the statement previously made. You have all probably heard about cases, or perhaps you know of some from your own experience, of peritonitis directly attributable to the overzealous relief of abdominal pain before a definite diagnosis has been made.

3. The cause of pain is important to determine. We all know that it is necessary to ascertain whether the cause of a headache is a brain tumor or some insignificant functional disturbance so that the cause (the tumor) may be removed. But I have in mind something less than that. From the standpoint of relief alone without removal of cause, a clear appreciation of the cause is often very helpful. For example, of three kinds of pain in the chest, the pain of intercostal neuralgia, the pain of effort angina and the pain of coronary thrombosis, differentiation is sometimes extraordinarily difficult. The agents which relieve one may be ineffective in the other. One can group other types of pain in that way; for example, pain in the legs due to myositis, vitamin B<sub>1</sub> deficiency or vascular disease. The effectiveness of the relief of the pain aside from the question of removing the cause depends here on a differential diagnosis.

4. The pathogenesis of pain is a matter of some importance; whether, for example, the pain is caused by spasm of smooth muscle or anoxemia or comes about as the result of inflammatory reactions around nerve fibers or endings.

5. The severity of the pain ought to be considered. Perhaps it is not sufficiently severe to require relief by therapeutic agents. Not infrequently when you are about to prescribe for a patient with pain the patient will ask you what the medicine is for, and you will say "For your pain." He may reply "I don't like medicines. I am not much interested in the relief of the pain so long as my mind is relieved that the cause is not



serious." Before we prescribe a drug, the question should be put whether the relief will recompense the patient for other forms of discomfort which the drug may cause. You will see patients taking two or three doses of codeine a day for the relief of very mild anginal pains. The price is disagreeable stupor and troublesome constipation. Such pains can often be much better controlled if we take the trouble to assist patients in making the necessary adjustments to reduce their activities to a level within their capacity without pain.

6. The natural course of the pain is also significant: Is it going to last a few hours or several days? Is it going to recur over long periods of time? Is it the kind of pain the intensity of which is likely to fall from its peak very gradually or is it likely to subside very abruptly? Morphine poisoning often arises from the use of large doses of the drug in patients in whom severe pain subsides abruptly. In such a case the morphine may seem to be producing very little depression, and the doses are repeated to secure more relief of the pain. With little warning, however, you find the patient lapsing into a state of profound stupor with depressed respiration, and you wonder what has happened. You have used large doses of morphine in a variety of pain which tends spontaneously to come to an end rather

#### *The More Common Analgesic Agents*

<i>A. Raise Thresholds</i>	
1. <i>Opium Group:</i>	
Morphine	5. Salicylates
Codeine	6. Magnesium Sulfate
Dilaudid	7. Sedatives
Pantopon	<i>B. Relax Smooth Muscle</i>
2. <i>Coal Tar Derivatives:</i>	1. Nitrites
Acetanilid	2. Xanthines
Acetophenetidin	3. Atropine
3. <i>Pyrazolon Compounds:</i>	4. Papaverine
Antipyrine	5. Calcium
Aminopyrine	<i>C. Special Mechanisms</i>
4. <i>Cinchoninic Acid Group:</i>	1. Trichlorethylene
Cinchophen	2. Ergotamine
Neocinchophen	3. Caffeine
	4. Vitamin B <sub>1</sub>

abruptly, leaving the patient under the influence of an amount of morphine which is toxic in the absence of pain, for pain is an antidote to morphine!

7. The psychic element in pain may vary anywhere from an insignificant role to the sole cause of the pain. That needs to be considered also from the standpoint of the kind of analgesic agents that are to be used. Fear and anxiety increase the perception of pain, and the use of small doses of sedatives greatly enhances the effectiveness of some of the analgesic agents. When reasonable procedures in a given case seem to be without influence on the pain, one might well ask whether the patient wants his pain relieved; the pain in this case may be one of the patient's most precious possessions. That needs to be considered before one goes on increasing the doses of drugs or shifting from one preparation to another in the endeavor to relieve it.

8. Finally, drugs are only adjuvants in the treatment of pain. Physical therapy, psychotherapy and specific cause treatment in the long run play the most important role in any program in which pain is the center of interest.

These are some of the important questions demanding consideration before one writes a single word of a prescription for the treatment of pain. We must not pretend, of course, that a clearcut answer will be always forthcoming, but I feel sure that if we ask those questions often enough we shall obtain a sufficient number of answers to make this sort of procedure extremely profitable.

Here is a list of the more common analgesic agents. It is not possible to make an altogether satisfactory classification of them. Perhaps this is as good as any, but you may think of a better one. The first group includes those agents which raise thresholds at the centers and block the perception of pain. The second includes those which relax smooth muscle and in that way abolish the impulses at their source. The third group includes substances which exert a specific action on certain kinds of pain: trichlorethylene, ergotamine, caffeine, vitamin B<sub>1</sub>. In some of these the mechanism is quite well established, in the case of others our knowledge is imperfect.

The more common clinical varieties of pain which present special problems are (1) headache, (2) visceral pain, (3) cardiac pain, (4) neuralgias, (5) root pains, (6) chronic arthritis, (7) dysmenorrhea, (8) labor pain. The list is not complete. We do not have the time this morning to go into all of these matters. Dr. Wolff is going to discuss some of the types of pain, and if any one has any special interest in others a discussion may be provoked by asking questions.

DR. CATTELL: Dr. Wolff will now take up the management of a specific type of pain.

DR. HAROLD G. WOLFF: I am going to discuss one type of pain, and that is headache; and just one variety of headache, namely migraine. I am selecting migraine to talk about for two reasons: 1. It is said to be the commonest clinical entity that civilized man happened to fall heir to. 2. I think that the management of migraine headache allows us to discuss the clinical approach to the problem of pain in general.

By migraine headache I mean the type of headache that is usually unilateral in onset, may become generalized, is associated with nausea and vomiting, sometimes with visual and other sensory disturbances, and usually occurs in families.

There are three ways of approaching this type of headache, as there are for other types of pain: first, by considering agents or procedures that act at the site of production of pain, for instance ergotamine tartrate, ergonovine, ephedrine, benzedrine, epinephrine, solution of posterior pituitary, ice cap, surgical ligation, resection and mechanical pressure; second, agents or procedures that act by raising the threshold of pain as, for example, codeine, morphine, acetylsalicylic acid, aminopyrine, acetanilid, phenacetin, ice cap; third, agents or procedures that act by lowering the blood pressure as in the case of glyceryl trinitrate or acetylcholine. I will disregard this third classification and limit our discussion to the first two.

Migraine results from the distention of some of the cranial arteries, chiefly the branches of the external carotid artery.

We know from our studies in the laboratory that a generalized headache can be produced with histamine, but after resection of the first division of the fifth cranial nerve such a headache will not appear in the part of the patient's head innervated by this division of the fifth nerve. Thus for clinical purposes we may consider the chief afferent pathway for headache to be the first division of the fifth nerve.

The method of investigation was as follows: The patient with a headache is put on a stretcher in a darkened room and a tambour over his temporal artery on the affected side records the amplitude of pulsations of the arterial walls. Records are made on a moving film in a camera.

In a representative patient with a migraine headache, ergotamine tartrate was given intravenously, and in the course of the next ten minutes the pulsations of the branches of the external carotid as recorded from the temporal artery had been reduced by 50 per cent and the headache had disappeared.

In another patient who received ergotamine tartrate (0.5 mg. intravenously) it happened to take about forty minutes for the headache to disappear, but again a parallel between the decline in the amplitude of pulsations of the temporal artery and intensity of the headache was demonstrated. A photograph was taken of this patient during the period of his headache, showing the large temporal vessels, both arterial and venous, standing out, which was in striking contrast to the flattened appearance of these vessels in a photograph taken immediately after the ergotamine had had its effect.

Records of pulsation of the cerebrospinal fluid, which represents the activity of the major spinal and the intracranial vessels, show variations in the height of pulsation which do not appear to be correlated with the headache or the disappearance of the headache after administration of ergotamine tartrate. Similarly, we have been able to demonstrate no correlation between the pressure of the spinal fluid and the headache. Thus I think we are at the moment justified in saying we do not know what role the branches of the internal carotid artery play in migraine headache, but such evidence as we have indicate it is not too important a role.

Photographs were taken of the retinal vessels before and after the administration of ergotamine tartrate. Although the veins appear to be a little smaller, I doubt whether there is much change in the arteries, although there may be a slight constriction.

Further, it can be demonstrated that ergotamine tartrate does not act in terminating headache by raising the threshold to pain. For instance, in one patient who had had his headache terminated by an intravenous dose of ergotamine tartrate an injection of 0.1 mg. of histamine produced the usual acute, the short-lived, histamine headache. This then indicates that the patient is just as able to perceive the headache after the administration of ergotamine as he was before.

In one patient the intramuscular injection of solution of posterior pituitary caused the headache to disappear, but the patient was white, was tremulous, complained of bad abdominal cramps and bad precordial pain, and I feared he might faint during the experiment. It is not a drug that one would care to give regularly, and it is not one that one can count on having a constant effect. It is not to be recommended.

Ephedrine sometimes succeeds in improving or eliminating a migraine headache, via the same mechanism: a reduction in the amplitude of pulsation of the cranial arteries. But the patient to whom it is given for migraine headache becomes tense and tremulous, and the disappearance of pain is often transient since at the end of four hours the headache may return with full intensity. Therefore, ephedrine cannot be considered as either a practical or a useful means of treating migraine headache.

In our experiments ergonovine, when successful, also eliminated headache by the same mechanism as did ergotamine tartrate. It contains more of the oxytocic property of the ergot drug, will abolish headaches in only about 50 per cent of trials, and cannot be relied on to be 100 per cent effective in reducing the amplitude of pulsations of cranial arteries.

Thus, if the agent employed succeeds in reducing the amplitude of pulsation of the cranial arteries by a sufficient amount, i. e. from 40 to 50 per cent, headache will be completely abolished, as is the case with ergotamine tartrate. It is thus evident that ergonovine hydracrylate cannot be regarded as an important asset in the treatment of migraine headache. Benzedrine sulfate, caffeine with sodium benzoate and pitressin are likewise unreliable in their effect on the magnitude of cranial artery pulsations and consequently in their effect on the headache. For instance, in two patients, caffeine with sodium benzoate (0.5 mg. intravenously) happened to increase the amplitude of pulsations and made the headache worse. Ergotamine tartrate subsequently reduced the pulsations by 40 per cent and eliminated the headache. Similarly, benzedrine sulfate reduced the amplitude of pulsations in another patient 25 per cent without reducing the headache, whereas ergotamine tartrate subsequently administered terminated it, and the amplitude of pulsations was seen to be reduced by 50 per cent. Ergotamine tartrate may at the moment be regarded as the most effective agent we have in reducing the amplitude of pulsations of the cranial arteries and terminating the migraine headache attack.

Before ergotamine tartrate was available, codeine was the best agent for stopping headache. One grain, or 60 mg., of codeine will stop most headaches, but how does it work? We observed a patient with migraine headache to whom 60 mg. of codeine was administered subcutaneously. As the headache disappeared the amplitude of pulsation of the cranial arteries did not change at all, an illustration that codeine does not act on the local pain-producing mechanism but raises the threshold to pain impulses arising from the stretched and dilated cranial vessels.

Codeine administered to another patient abolished his headache, again with no change in the amplitude of cranial artery pulsations. This patient soon complained that his headache had returned with about 50 per cent of its original severity. We then gave him ergotamine tartrate, the headache disappeared promptly, and the cranial artery pulsations, although they had not changed during this whole period when the headache had been transiently relieved by codeine, were now reduced in amplitude by over 50 per cent. His migraine attack proved to be successfully terminated.

How should one manage an acute migraine attack? The patient should retire to a darkened room and remain in bed for at least two hours, and 0.5 mg. of ergotamine tartrate should be given intramuscularly as soon as it is feasible to give the drug after the onset of the headache. This drug when given intravenously will produce quicker results; that is, it takes about thirty to fifty minutes to produce effects through the intramuscular route and about ten to forty minutes by the intravenous route. Giving ergotamine tartrate by the mouth should be avoided for two reasons: 1. It eliminates the headache only about 50 to 60 per cent of the time. 2. Patients may be induced to take it too often. Patients may have the tendency to take a few pills by mouth "every once in a while." If it is necessary to give it by mouth for reasons best known to you at the time, give 3 mg. followed by 2 mg. an hour until the headache has disappeared or a total of 11 mg. has been given. However, I am not enthusiastic about this procedure.

Suppose the patient feels as though he is about to have a migraine attack, is there anything you can do

to stop it from developing? Usually not, but you might try. The patient can be urged to go to bed and 3 mg. of ergotamine tartrate may be placed under the tongue. This will be absorbed in a few minutes and sometimes will stop the headache when repeated in 2 mg. doses hourly until 11 mg. has been given. If it does not, you are in a dilemma because you have already given ergotamine tartrate and you do not know how much more to give by the more successful intramuscular or intravenous route. I am not in favor of ergotamine tartrate by mouth. Some report the successful use of a mixture of acetanilid and sodium amytal, although I never used it and I do not know how effective it is. In any event the patient should stay in bed for two hours after such medication. Many times patients feel they are going to get a headache and don't, so you never know whether this kind of procedure is efficient or not, but you can try it and see what happens.

Don't give ergotamine tartrate more often than once a week to patients with cardiovascular disease, with or without hypertension, including those with Raynaud's syndrome, venous thrombosis, syphilitic arteritis and coronary disease; to patients with sepsis or fever; to patients with hepatic or renal disease; to pregnant women. Fortunately, most pregnant women stop having migraine attacks during their pregnancy, and the occasional woman can take ergotamine late in the pregnancy without danger; but never give ergonovine hydracrylate under any circumstances to a pregnant woman. Lastly, do not give ergotamine tartrate to badly nourished or cachectic persons. It is said that persons deficient in vitamin C do badly with ergotamine, and a poorly nourished person probably has such a vitamin deficiency. Finally, remember that in treating migraine headache you are treating the acute episode of pain and not the syndrome of migraine.

STUDENT: What is the length of time that a patient with migraine gets relief from one injection of ergotamine?

DR. WOLFF: It terminates the attack. Attacks usually last from a few hours to a few days. The administration of ergotamine does not shorten the interval between attacks. The management of the frequency of these various attacks must be through other means than ergotamine. Ergotamine simply terminates any given attack.

STUDENT: I should like to know the mode of action and effectiveness of trichlorethylene.

DR. WOLFF: Trichlorethylene is useful in pains of the face of any kind. It is not known what the exact site of action is, but it seems to raise the threshold for all types of pain about the head. Its chief usefulness is in trigeminal neuralgia. I think that was discovered, as you probably know, during the war when it was used as a solvent for certain airplane coverings, and the workers in the airplane factories were being poisoned, so that they became anesthetic about the face.

STUDENT: Has it any effect on pains elsewhere?

DR. WOLFF: I do not believe so but I am not certain.

DR. CATTELL: In the past we have been fortunate in having the collaboration of representatives from various clinical departments in connection with our conferences. The list that was put on the board by Dr. Gold includes a number of conditions which might be discussed further. I wonder if there is any one here from the Department of Obstetrics and Gynecology who might be willing to say something about the topics

dysmenorrhea and labor pain. The question of arthritis is another important topic.

DR. ANDREW A. MARCHETTI: I will talk about the first one. Dysmenorrhea is the pain in menstruation. As you know, dysmenorrhea is either congenital, functional or acquired. I think that of course the most important thing to do is to find out what can ease dysmenorrhea. Most of the time our therapy is pointed toward patients with dysmenorrhea who have either hypoplastic, that is, more or less infantile, generative organs or a malposition, acute antelexion and acute retroflexion. In those instances we give them so-called compound powders of atropine and codeine. Each powder contains 16 mg. of codeine sulfate and 0.25 mg. of atropine sulfate, as well as 160 mg. of acetylsalicylic acid and acetophenetidin. Patients are usually instructed to take the powders every four hours when they expect the pain, and usually two or three will relieve pains which are associated with the menstrual period. In instances we have used codeine, but as a rule that does not do as well as the compound powders of atropine. As Dr. Gold pointed out, the atropine is supposed to bring about relaxation of smooth muscle. It does help, especially in case of acute antelexion. It is not 100 per cent effective, of course, and it is less effective in the patient with a hypoplastic uterus.

Some of the nitrites have been used for dysmenorrhea, but I do not believe they are used as commonly as atropine and codeine.

In the acquired dysmenorrhea it may be a uterine or ovarian tumor, an inflammatory disease or a flare-up of salpingitis which causes the pain. Peritoneal or abdominal tumors that press on the uterus itself cause pain which is not elicited until the patient is about to have a period. A uterine or ovarian tumor may cause pain in the intermenstrual period.

Then too the cachectic or the undernourished person may complain of dysmenorrhea. You will find them anemic, and when they are built up by good food, fresh air, and the things we commonly have at our disposal for nutritional disturbances, usually the pain at menstrual time disappears.

Are there any questions that you wish to ask?

DR. GOLD: I wonder how deep is the conviction with regard to atropine for easing menstrual pain. A quarter of a milligram is a mighty small dose, and I am not sure that with such a dose it will be ever possible to demonstrate any physiologic effect.

There is a question I should like to ask as to codeine.

Are you ever worried about the possibility of drug addiction since these patients take it repeatedly over long periods of time?

DR. MARCHETTI: I have never seen that. I know Dr. Kelly in Baltimore is very apprehensive about drug addiction. I asked him about it and he said he had never seen it except on one or two occasions when patients became addicted to codeine. The drug is only a temporary measure. Usually, if the dysmenorrhea is severe enough, whether it is acquired, functional or congenital, the patient comes back. In the malpositions, let us say, we insert a pessary and give the patient a therapeutic test. If the retro position is relieved by putting the uterus in its normal position or approaching that, we then know the cause of the dysmenorrhea and eventually the patient will get a suspension.

DR. GOLD: I understand that aminopyrine is widely used in dysmenorrhea. Would you care to comment on this?

DR. MARCHETTI: We discourage its use, particularly because of the danger of agranulocytosis. It does relieve the pain but not as effectively as the compound powder of atropine and codeine.

DR. CATTELL: We have a small amount of time remaining for discussion, and there may be questions relating to some of the specific conditions mentioned. It seems to me this is an unusual opportunity to ask questions of men who have given special thought to the particular problems under discussion, and we should like to have all the students participate.

STUDENT: I have heard of the use of benzyl benzoate in dysmenorrhea, and I was wondering whether there was anything to it.

DR. MARCHETTI: It helps in some instances. I do not think it is as effective as the codeine and atropine.

STUDENT: I should like to ask Dr. Gold how large a dose of morphine may be given to control pain in coronary thrombosis.

DR. GOLD: You cannot give more than a quarter of a grain of morphine ever entirely safely. One gives as high as three quarters of a grain or even a grain, but if so one may expect to get into serious difficulties at times because coronary thrombosis is a classic illustration of very severe pain which tends to descend from its peak rather abruptly. If you give a quarter of a grain and the pain is not relieved, then within a half to three quarters of an hour you give another quarter and another quarter; perhaps by the third or fourth dose the pain may subside rather abruptly and at the same time you have a patient in fairly deep narcosis, in whom the pain had previously served as the antidote to the toxic effects of the morphine.

DR. CATTELL: I should like to ask Dr. Angevine whether there are some points in the management of arthritis that it might be profitable to discuss.

DR. D. MURRAY ANGEVINE: I think practically every drug has been used in the treatment of arthritis. I will mention just two types, rheumatoid arthritis and osteo-arthritis. The latter is apparently not related to infection. The ideal treatment for arthritis, just as for rheumatic fever, is rest. Sometimes it is impossible to provide rest, so we must do the best we can. We find that salicylates are of value in arthritis, but I think that is a rather general statement. We all use them because we know of nothing better, but practically 60 per cent of the patients that I see in the clinic will say "I took aspirin, but it did not help me." Rheumatic fever, of course, is an entirely different proposition. Our big agent for the treatment of arthritis, aside from rest, is physical therapy, and there are numerous methods by which it can be applied.

There are two points that may be of interest. It has been observed that patients with rheumatoid arthritis who became jaundiced become free from pain. This has been applied experimentally and about one half of the people who are jaundiced artificially are free from pain. It is obvious that such a method cannot be generally applied. However, such an observation is of value in that it may give us an indication as to the mechanism of pain in arthritis. In view of Dr. Wolff's statement that pregnancy relieves migraine it is of some interest that in a series of thirty pregnancies in patients with rheumatoid arthritis practically all were relieved of pain during their pregnancy. In fact, one woman said that she had gone through four pregnancies, and during them she was entirely relieved of her arthritis.

DR. ARTHUR P. RICHARDSON:<sup>1</sup> Pain is, of course, without a doubt the principal reason for patients coming to doctors. It is the thing that patients usually want to be relieved of. They are not particularly interested in what the mechanism is, all they want is relief from their pain. I am not at all sure of the quotation of Pasteur, but I believe it runs like this: "We would cure few, relieve many, and comfort all." That is beyond doubt the outstanding duty of all doctors, at least from the point of view of the patient.

DR. JOSEPH C. HINSEY: I have been concerned with mechanisms involved in pain rather than with drug effects on pain. However, I have been very much interested in this discussion. There are two or three points that occur to me. First, in the use of drugs which raise the threshold to pain, we are dealing with effects on peripheral or central mechanisms, and probably both. It should be emphasized that the peripheral pathways traverse the dorsal roots of spinal nerves and the sensory roots of cranial ones. There are no afferent pathways aside from these.

In dealing with drugs which attack the efferent nervous mechanisms or smooth muscle directly, the phenomenon of relaxation of smooth muscles is a very important factor in the relief of pain. In Dr. Wolff's description of the relief of migraine by ergotamine tartrate and other drugs, the pulsations in the branches of the external carotid artery were reduced. I do not know what changes in the state of the smooth muscles of the arterial walls accompanied this reduction. However, in conditions in which pain is produced by anemia and the resultant anoxia in tissues, relaxation of smooth muscle in the vascular bed induced by the action of drugs leads to an improvement of blood supply and helps to relieve pain. In physical therapy, counter-irritation may relieve pain by the induction of reflexes that relax smooth muscle both at the periphery and in the viscera, producing among other things an improvement of blood supply.

Second, there is one other place where drugs are used in the problem of pain that is of interest at the present time; that is, in the field of diagnosis. The use of local anesthetics in the blocking of peripheral and visceral nerves gives information as to the possible relief to be obtained in painful syndromes by surgical procedures. Recently, Livingston has reported ten cases of atypical pain in the extremities produced by trivial injuries. He found that he could relieve pain by the use of local anesthesia at the periphery in the "trigger" zones and also by blocking the sympathetic trunks. It seems to me that the use of local anesthetics such as procaine hydrochloride has an important role in the attack on a number of types of atypical pain.

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1. Dr. Richardson is National Research Fellow, the Johns Hopkins University.

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**Political Career of Claude Bernard.**—The year 1860 saw the beginning of Bernard's political career, which was, indeed, short but which occurred at an exciting moment in the history of his country. An imperial decree of May 6 made him a senator. His yearly income was in consequence augmented by 30,000 francs and there is still among his relics at Saint-Julien a card bearing five stamps, which shows that he received five quarterly payments of his stipend. . . . Bernard took his duties as senator seriously, as he did all obligations which he assumed. There is not a day's balloting recorded in the official journal after Bernard took his seat in August 1869 which does not include his name.—Olmsted, J. M. D.: Claude Bernard, Physiologist, New York, Harper & Bros., 1938.

## Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING ARTICLE AND REPORT.

HOWARD A. CARTER, Secretary.

### PHYSICAL CHARACTERISTICS OF SHORT WAVE DIATHERMY

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MINNEAPOLIS

In former articles<sup>1</sup> the physical and biophysical aspects of the older type of long wave diathermy have been discussed. These previous articles contain descriptions of the methods whereby the low frequency 25 to 60 cycle alternating current may be converted into high frequency diathermy current by means of the spark gap diathermy machine or the vacuum tube apparatus. This older type of diathermy current is that which has a frequency between 500 and 2,000 kilocycles per second and is applied to the patient by contact electrodes. Since a discussion of long wave diathermy has already been given, and since the main interest today is in short wave diathermy, the present article will be confined almost exclusively to short wave diathermy except when comparisons are to be made with the older form of diathermy.

It is of historical interest that during the past year a friendly controversy has arisen as to the priority of the discovery that high frequency alternating electric currents could traverse irritable tissues without electrical shock. The clinical use of diathermy as a mode of therapy followed soon after this discovery. According to Bordier,<sup>2</sup> d'Arsonval, Claude Bernard's successor at the University of Paris, commenced in 1881 a study of the stimulating effects of electric currents of varying frequency. d'Arsonval built an oscillator capable of producing alternating currents of frequencies as high as 10,000 cycles a second and demonstrated to his classes at the university in 1889 that at the higher frequencies the current for stimulation had to be increased. Following the discoveries of Hertz, d'Arsonval used the hertzian oscillator (the spark gap circuit) for frequencies above 10,000 cycles. These results were published in 1891 and first presented at meetings of the Society of Biology at Paris at its sessions of Feb. 24, April 25 and May 2, 1891. Nikola Tesla, an Austrian physicist in the United States, was studying illumination produced by high frequency currents and noted that high frequency currents of sufficient intensity to cause illumination did not produce neuromuscular stimulation. These observations of Tesla were published May 23, 1891. The conclusion to be drawn from this interesting note of Bordier's is that the discoveries were made almost simultaneously and were published in 1891. This year may be regarded as the beginning of the development of diathermy.

### SHORT WAVE DIATHERMY

Since 1930 there has arisen a continuously increasing interest in short wave diathermy, stimulated by many clinical reports of its beneficial therapeutic use and a large amount of advertising by manufacturers of apparatus. This new form of therapy has been greeted with much enthusiasm by some investigators as a discovery of major importance. The *British Journal of Physical Medicine*<sup>3</sup> states "It is no exaggeration to call short wave diathermy the greatest discovery in physical medicine since the work of Roentgen." Other investigators, particularly those in America, have been less enthusiastic about the merits of short wave diathermy and believe it to be solely a unique and useful method of applying heat. Conventional diathermy, or long wave diathermy, has been used with success for many years and short wave diathermy can be regarded only as a new and improved mode of therapy if it has definite proved advantages over the older type. It is our purpose in this review to describe the method of production of short wave currents and then to discuss the advantages and disadvantages of the newer form of diathermy in comparison with the older form.

### A TYPICAL OSCILLATOR CIRCUIT

There are several typical circuits for the generation of short wave diathermy currents. These may be divided into two groups: those which produce the longer of the short wave diathermy currents, i. e. frequencies in the range from 10 to 100 megacycles (from 30 to 3 meters), and a second group producing frequencies greater than 100 megacycles. As a typical oscillator of the first group, the simple two-tube "push-pull" circuit will be described. This type of oscillator for production of long wave diathermy currents (1 megacycle per second) has been described by Hemingway and Witts.<sup>4</sup> The same typical current may be used for the generation of higher frequencies.<sup>5</sup> This entire circuit can be considered to consist of three essential parts, (a) the power supply, (b) the oscillating circuit and (c) the output circuits.

(a) *The Power Supply.*—The high frequency current in short wave diathermy machines is generated by a vacuum tube oscillator circuit which usually consists of one or two vacuum tubes with an appropriate circuit of inductances and capacities. The thermionic vacuum tubes are evacuated glass bulbs containing a filament, grid and plate. The filament is heated to incandescence by a low voltage alternating current of the same frequency as the input current, i. e. from 25 to 60 cycles per second. A high direct current voltage of from 100 to 1,000 volts is applied between plate and filament, the plate being made positive and the filament negative. It is the function of the power supply to furnish the low frequency low voltage alternating current to heat the filament of the vacuum tubes and to supply the high direct current voltage to draw electrons from the filament to the plate. The power supply unit consists of one or two transformers, two or four rectifier vacuum tubes and sometimes a condenser. For simplicity a four tube rectifier will be described, but this may be

1. G. Hemingway, Allan, and Stenstrom, K. W.: Physical Characteristics of the Older Type of Long Wave Diathermy, *J. A. M. A.* 98: 1446 (April 23) 1932; (b) *Physical Characteristics of Diathermy and Short Wave Diathermy*, *Phys. Ther.* 10: 105 (Nov. 2) 1935.  
2. Bordier, J. L.: *Arch. Phys. Therapy* 19: 109 (Feb.) 1938.

3. The Greatest Discovery, editorial, *Brit. J. Phys. Med.* 8: 127 (Dec.) 1933.

4. Hemingway, Allan, and Witts, G. H.: A High Frequency Apparatus for Producing a Measured Heat Stimulus in Studies of Physiological Temperature Regulation, *Physics* 7: 299, 1936.

5. Bishop, F. W.: An Apparatus for the Production of Local Heat in Body Tissue by Means of High Frequency Electrical Fields, *Radiology* 21: 487 (Nov.) 1933.

replaced by one with two tubes which functions as the described four tube type.

One transformer converts the 110 volt 60 cycle current to low voltage 4 to 10 volt 60 cycle current to heat the filament of the vacuum tubes. This is a "step-down" transformer. The other one is a "step-up" transformer and converts the 110 volt 60 cycle current into from 500 to 1,000 volt 60 cycle current. This high voltage current in some machines is "rectified," as will be described, or in other machines is delivered as high voltage alternating current to the oscillator tubes.

The rectifier system, if present, consists of two or four rectifier tubes. A four tube rectifier is shown in figure 1 and consists of four diode tubes. The two tube rectifiers function in the same manner but two tubes are combined into one. These diode tubes each contain a filament and plate and permit electrons to flow only in one direction—from filament to plate—and in this way behave as thermionic valves. An electron current flows only when the plate is positively charged with respect to the filament. When the plate is positive the negatively charged electrons which are emitted by the filament move to the plate, the stream of particles forming the current. When the filament is made positive and the plate negative no current flows, since the current through the tube is carried only by the negatively charged electrons. In figure 1 the arrows indicate the

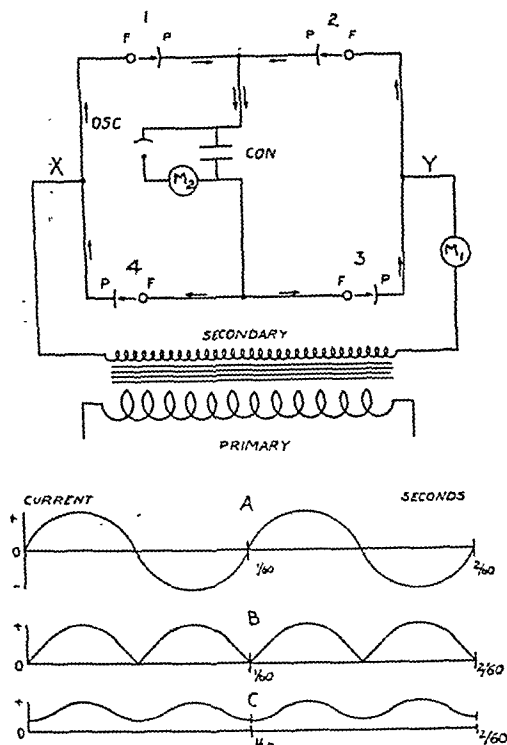


Fig. 1.—Action of full wave rectifier in power supply unit of an oscillator. *F P*, filament and plates of rectifier tubes, 1, 2, 3, 4. *Osc*, vacuum tube in oscillator circuit to which rectifier supplies a high direct current voltage output. *Con*, condenser of high capacity connected in parallel with direct current output of rectifier. *A*, alternating current from transformer secondary as indicated in ammeter *M*<sub>1</sub>. *B*, rectified current flowing in output circuit as measured in ammeter *M*<sub>2</sub> without condenser (*Con*) in circuit. *C*, output current from rectifier as measured in *M*<sub>1</sub> with condenser (*Con*) connected as shown.

direction in which the current flows through the tubes. A high voltage alternating current is supplied to the rectifier system by the step up transformer. This current, which passes through meter *M*<sub>1</sub>, is indicated at

curve *A*. The positions *x* and *y* are subjected to an alternating potential, which varies in a cyclic manner. When *x* is positive *y* is negative and  $\frac{1}{120}$  second later *x* is negative and *y* is positive. When *x* is negative and *y* is positive the electron current flows over the path  $x \rightarrow 1 \rightarrow osc \rightarrow 3 \rightarrow y$  and no current flows through tubes 2 and 4 on account of the electronic action of the

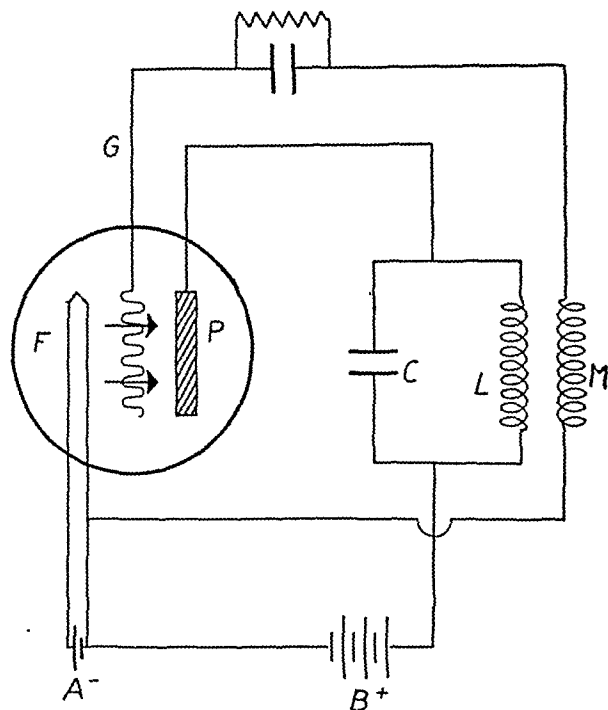


Fig. 2.—Simple oscillator circuit. *F*, filament; *G*, grid; *P*, plate; *C*, condenser; *L*, inductance; *M*, grid meter; *A*, direct current voltage applied to plate; *A*, current.

valve. During the next half cycle when *x* is positive and *y* negative the current flows over the path  $Y \rightarrow 2 \rightarrow osc \rightarrow 4 \rightarrow X$  and no current flows through tubes 1 and 3. In both instances the current from the rectifier, that is, the current supplied to the oscillator (*osc*) and measured by meter *M*<sub>2</sub>, flows in one direction. Without the condenser (*con*) the unidirectional current from the rectifier would pulsate as shown in curve *B*. The presence of the condenser (*con*) smooths out the pulsations to give an output current as indicated by curve *C*. The condenser acts as a storage place for the electrical charges that enter and leave while rapid changes of current are taking place. This condenser has a tendency to produce a uniform flow in much the same way as that in which the elastic walls of the large arteries take up the pressure pulse and produce an even flow of blood.

(b) *The Oscillator Circuit*.—This consists of a three electrode vacuum tube containing filament, grid and plate connected in a circuit containing a condenser *C* and an inductance *L*, as shown in figure 2. A stream of electrons is drawn by the high voltage from the heated filament to the plate through the grid. The magnitude of this current is controlled by the grid voltage and plate voltage. The closed circuit containing *C* and *L* has the important property of having an alternating current produced within it under the conditions shown. The frequency of the alternating current is determined by the capacity of the con-



denser and the inductance ( $L$ ) according to the formula  $f = \frac{1}{2\pi\sqrt{LC}}$ , in which the inductance depends on the size and number of turns of the coil and the capacity ( $C$ ) depends on the distance between the condenser plates and on their areas and number.<sup>1b</sup> It is to be noted that as the capacity and inductance decrease the frequency increases. With short wave oscillators the capacity and inductance are very small. The plate and filament are made of metal. They are separated by a vacuum and behave as a condenser, which is in parallel with  $C$ . Usually this interelectrode capacity is small, but when very short wave radiation (high frequency) is to be produced it is this factor which sets an upper limit to the frequencies that can be produced. In some circuits this is the only capacity in the oscillation circuit. The oscillating current in the

$LC$  circuit induces voltage changes in the coupling inductance ( $M$ ), which are impressed between the grid and the filament and produce fluctuations of the same frequency in the plate current. This phenomenon is called the "grid feed back" and is responsible for the "regeneration" or maintenance of a sustained oscillating current in the  $LC$  circuit.

(c) *The Output Circuit.*—This circuit of the short wave apparatus contains the electrodes or coils which are applied to the patient in addition to a variable condenser, an inductance and a meter. The output circuit is represented on diagram III in figure 3, which shows an assembled short wave diathermy circuit, including the power supply (diagram I) and the oscillator circuit (diagram II). The external

tubes is shown in diagram I, where the bridge method of rectification, as shown in figure 1, is used. The leads  $A$  in figure 3 carry current to heat the filaments of the oscillator tubes 5 and 6. The leads  $B$  carry the high voltage rectified current,  $B+$  being connected to the plate and  $B-$  to the filament of the oscillator tubes. Diagram II of figure 3 shows the main oscillating circuit and its connections. This oscillating circuit is a widely used two tube oscillator type which gives added power and stability, but the principle of operation is the same as the simpler circuit of figure 2. Actually there are many modifications of this typical circuit in use today but the general scheme is the same for all. This type of machine may be used for both long and short wave diathermy current. A similar device has been described by Bishop.<sup>5</sup>

#### CHARACTERISTICS OF SHORT WAVE DIATHERMY CURRENT

(a) *Position of Electrodes.*—When long wave diathermy is used, it is necessary to place the electrodes in contact with the skin. In many treatments this is a satisfactory procedure but in some cases it is unsatisfactory, especially when a large electrode is to be used over some irregular surface in which there are bony projections. With short wave diathermy it is possible to place an insulating pad or to interpose a layer of air between electrode and cutaneous surface, or one may use a coil of fairly rigid insulating cable wrapped around a limb but at some distance from the cutaneous surface. By applying short wave electrodes at a distance, it is possible to heat the desired region without causing irritation of the skin. According to Cumberbatch<sup>6</sup> it is this characteristic of the short wave diathermy that is responsible for the beneficial effects in acute infections of the skin and subcutaneous regions. Krusen<sup>7</sup> states that the difference between the long wave and the short wave diathermy is the convenience of the short wave technic.

The reason contact electrodes must be used with long wave diathermy whereas distant electrodes may be used with the short wave apparatus is the differences in frequency between the two types. Figure 4 represents a conducting tissue between two short wave diathermy electrodes with an air space separating the tissue from the electrodes. The equivalent electrical circuit is also shown. Part of the current passes between the condenser plates as a wattless current indicated by  $I_1$ . The conduction current that heats the tissue flows through the resistance  $R$ . The system of tissue-air space-electrode at each electrode behaves as a condenser. The impedance of this condenser  $C_2$  is given by the fraction  $1/\text{frequency} \times \text{capacity}$ . The capacity may be increased by bringing the electrode closer to the tissue, since the capacity is inversely proportional to the thickness of the dielectric, in this case air. The impedance to the high frequency current may be reduced by increasing the capacity and increasing the frequency. Hence increasing the frequency allows more current to pass through this condenser and through the tissue. There is some belief that the mechanism of heating and current conduction is different in the two types of diathermy. There is no basis for this belief. The current through tissue consists of oscillating charges. Increasing the frequency causes the ionic

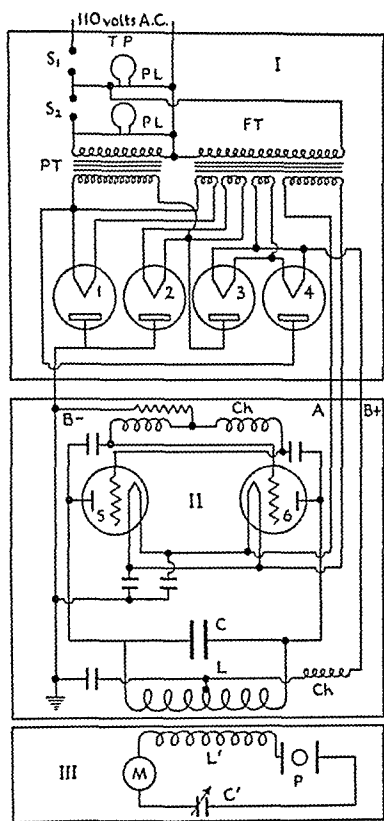


Fig. 3.—Circuit for the production of short wave diathermy current; I, power supply; II, oscillator circuit; III, output circuit;  $S_1$ ,  $S_2$ , switches;  $PL$ , pilot lamp;  $FT$ , filament transformer;  $PT$ , plate transformer; 1, 2, 3, 4, rectifier tubes; 5, 6, oscillator tubes;  $C$ ,  $L$ , capacity and inductance in main oscillating circuit;  $C'$ ,  $L'$ , capacity and inductance in external output circuit;  $M$ , ammeter for measuring current in output circuit;  $P$ , tissue heated;  $B-$ ,  $B+$ , direct current voltage to plate filament of oscillator tubes;  $A$ , low voltage alternating current leads for heating filament of oscillator;  $Ch$ , choke coil.

circuit containing the patient is inductively coupled to the main oscillating circuit  $LC$ . Current in this external circuit is increased or decreased in one of two ways, either by "tuning," i. e. varying the capacity of the output circuit, or by changing the coupling between the output circuit and the main oscillating circuit. By changing the coupling the two inductances  $L$  and  $L'$  are brought closer together, thus increasing the current in the external circuit.

The assembled circuit is shown in figure 3. The power supply, including transformers and rectifier

6. Cumberbatch, E. P., and others: Discussion on Short Wave Therapy, Proc. Roy. Soc. Med. 20: 211 (Jan.) 1937.  
7. Krusen, F. H.: The Present Status of Short Wave Diathermy, J. A. M. A. 110: 1280 (April 16) 1938.

displacement to be less and the rapidity of oscillation greater. If a long wave diathermy machine were connected to short wave electrodes, with an air space between electrodes and tissue, a current would flow but it would be small because of the high impedance of the air space and would be insufficient to cause appreciable heating.

(b) *Measurement of Temperature.*—One of the reasons why so little progress has been made in determining the temperature distribution of animals or patients treated with short wave diathermy is that it is not possible to measure the temperature of a heated tissue by a thermocouple or a mercury thermometer during the passage of the current. These metallic temperature measuring devices when placed in a short wave electrical field behave as receiving antennas and foci for the short wave current. In measuring the temperature of a tissue heated by short wave diathermy the customary procedure is to shut off the diathermy current and insert the thermocouple needle into the heated tissue. In the time interval between the shutting off of the current and the final equilibrium deflection of the galvanometer a considerable fall in temperature may occur, especially in a vascular region. Using long wave diathermy to heat a vascular region of the brain of dogs and placing fine wire thermocouples between electrode and brain tissue, we have noted a drop of 3 degrees centigrade in half a minute after the diathermy current was turned off.<sup>8</sup> With long wave diathermy it is possible to measure the temperatures of the heated tissue while the current is flowing. Thermocouples may be used to measure long wave heating effects provided proper precautions are observed as to galvanometer shielding, use of choke coils and position of the thermocouple in the field, according to Stenstrom and Nurnberger<sup>11</sup> and Hemingway and Hansen.<sup>9</sup>

(c) *Measurement of Dosage.*—With long wave diathermy, clinical experience over many years has established definite dosages that are recommended for treatment. These dosages are prescribed in terms of the current density of the smaller diathermy electrode, with 100 milliamperes per square inch of the smaller electrode recommended as the maximum. If the diathermy current passes through a constricted region smaller than the area of the smaller electrode, this dosage must be reduced, as, for example, heating through a knee joint with electrodes above and below the knee.

For many years it was believed that the diathermy current measured by the meter of the long wave machine was not a true heating current. It was believed that a part of the current registered by the ammeter was "wattless" in that it did not produce heat within the tissues. It is theoretically possible that a current passing through the tissues between diathermy electrodes should have a "conduction" component which is responsible for the heating and a "wattless" component which passes across the electrodes as through a condenser, the so-called displacement current. d'Arsonval<sup>10</sup> made measurements of the heat production in solutions heated by long wave diathermy and stated that a large fraction of the total current

was wattless. The significance of this observation by d'Arsonval was that it made dosage measurements of long wave diathermy impossible, since a dosage stated in milliamperes per square inch would be useless if a large fraction of the current was wattless. This problem was reinvestigated by Hemingway,<sup>11</sup> and measurements were made of the resistance and phase angle by Hemingway and McClendon<sup>12</sup> of tissues heated by long wave diathermy. It was shown that under clinical conditions the current as registered by the diathermy ammeter was almost entirely conduction current, the wattless component being negligible. In the highest frequencies of the long wave diathermy region, e. g. 2 megacycles per second, the wattless component could be 5 per cent of the total diathermy current.

With short wave diathermy it is not possible to designate dosage in terms of diathermy current which would be applicable to all types of treatment. The reason for this is that as the frequency increases from the long wave range, 0.5-2.0 megacycles per second, to the short wave range, 10-100 megacycles per second, the wattless component of the current increases. The wattless component is increased still more when the electrodes are used at some distance from the skin

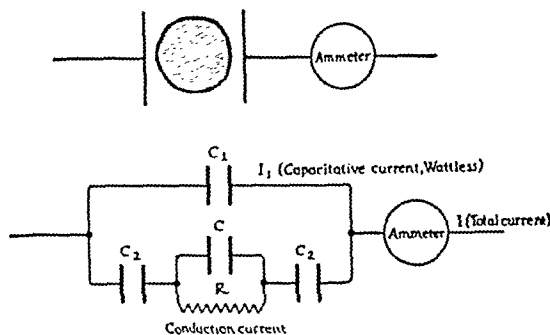


Fig. 4.—Electrical equivalents of tissue between short wave diathermy electrodes.

and varies with shape, size and position of the electrodes. The dosage must be regulated by experience as judged by the sensation of heat in the patient. Once a dosage calibration on this patient's tolerance basis has been established one can assume that for a given position, size and shape of electrode and shape, size and position of the region of the body heated the wattless component remains the same and that the electrical conditions can be repeated.

(d) *Temperature and Heat Distribution.*—1. Experiments on Solutions and Dead Tissues: A striking characteristic of short wave electrical fields is that, when the field intensity is kept uniform and electrolytic solutions of various concentrations in test tubes are placed in the field for the same length of time, the rate of heating for the different solutions varies. This effect as described by Hosmer<sup>13</sup> has been verified by others and shown by McLennan and Burton<sup>14</sup> and Pätzold<sup>15</sup> to be a direct consequence of the physical laws governing the heating of electrolytic solutions. According to

11. Hemingway, Allan: Thermal Effects of Diathermy. *Radiology* 14: 99 (Feb.) 1930.

12. Hemingway, Allan, and McClendon, J. F.: The Measurement of the Heat Production in Diathermy. *Physics* 4: 351, 1933.

13. Hosmer, Helen: Heating Effects Observed in High Frequency Fields. *Science* 68: 325 (Oct. 5) 1928.

14. McLennan, J. C., and Burton, A. C.: The Heating of Electrolytes in High Frequency Fields. *Canad. J. Research* 3: 224 (Sept.) 1930.

15. Pätzold, Johannes: Die Erwärmung der Elektrolyte im hochfrequenten Kondensatorfeld und ihre Bedeutung für die Medizin. *Ztschr. f. Hochfrequenztechnik* 26: 85, 1930.

8. Stenstrom, K. W., and Nurnberger, Paul: Effect of Diathermy Treatments on Temperature. *Arch. Int. Med.* 44: 556 (Oct.) 1929.

9. Hemingway, Allan, and Hansen, C. O.: Temperature Distribution in Local Diathermy Treatments. *Radiology* 17: 1258 (Dec.) 1931.

10. d'Arsonval, J. A.: L'échauffement des tissus par les courants de haute fréquence. *Compt. rend. Acad. d. sc.* 185: 324, 1927.

electromagnetic theory, and supported by experimental observations, the rate of heating of a solution in an electrical field between the electrodes of a short wave diathermy machine depends on the frequency (or wave length) of the alternating electrical field. At a particular frequency, the rate of heating is a maximum. The frequency at which the maximum heating takes place is related to the electrical conductivity and dielectric constant by the formula

$$\text{frequency} = \frac{2 \times \text{specific conductivity}}{\text{dielectric constant}}$$

The various tissues of the human and animal body have specific conductivities which vary widely.<sup>16</sup> Schereschewsky<sup>17</sup> has shown, however, that the dielectric constants of different tissues are practically equal to that of water, 76-78, with the exception of fat, which has a low value of 13.6. The theory would predict that different tissues with these widely varying electrical conductivities would each have a certain specific wavelength at which maximum heating would take place in the high frequency fields. That such maximum heating effects for various tissues do actually occur have been shown by Schereschewsky,<sup>17</sup> McLennan and Burton,<sup>18</sup> Bachem<sup>19</sup> and others. These were dead tissues usually isolated from other tissues in glass containers. There is, however, a considerable lack of agreement among the various investigators as to what wavelength produces a maximum heating effect for a particular tissue. As an example, according to Coulter and Osborne,<sup>20</sup> three different investigators have reported three different wavelengths for the maximum heating of fat, namely 14.5, 3 to 10 and 5 meters. One may conclude that the maximum heating effect for a particular dead tissue does occur for a definite wavelength but that it is variable with the tissue and technic of measurement. Selective heating of a tissue for a particular wavelength has been observed in dead limbs by Schliephake<sup>21</sup> and McLennan and Burton.<sup>18</sup>

Basing these observations on these demonstrations of selective heating of dead tissues, either isolated or in situ, some authors have assumed that this selective heating action applies to tissues in living warm blooded animals. Such assumptions without experimental proof are entirely unwarranted. Those controlled experiments which have been performed for the purpose of investigating this particular problem have shown no selective action, at least in the tissues of human beings.<sup>22</sup>

2. Experiments on Living Animals and Man: As a result of the interesting studies on selective heating as a function of the wavelength of solutions and tissues in vitro, the results of temperature distribution in living tissues becomes a problem of prime importance. The

differences between dead excised tissues and living tissues in situ are that: 1. There is in the living body a powerful equalizing action exerted on the tissue temperature by the circulating blood. The importance of this was well demonstrated by Binger and Christie<sup>23</sup> for long wave diathermy. These investigators showed that the circulation through a locally heated region tended to reduce any local rise in temperature. 2. A tissue in situ is in contact with and surrounded by other tissues. These neighboring tissues, which may be good conductors, such as muscle and plasma, tend to exert a "shielding" effect. The heating of a particular tissue such as bone in a living animal is quite a different problem from the heating of bone in a test tube surrounded by glass or air. The measurements of Mortimer<sup>24</sup> have indicated the importance of the equalizing effect of blood flow on temperature of the visceral organs of dogs heated by short wave diathermy. Mortimer and Osborne,<sup>22</sup> Coulter and Carter<sup>25</sup> and Coulter and Osborne<sup>25</sup> have measured the increase in temperature at various sites in human subjects, using short wave diathermy currents of wavelengths from 6 to 24 meters, and have reached the conclusion that there is no specific or selective heating shown that varies with the wavelength. It would seem from their work that one wavelength is as good as another.

#### CONCLUSION

We wish to emphasize the need for more investigations on the controversial problems, especially the so-called athermic effects. More work is needed on the temperature distributions in various living tissues and the development of better methods of thermometry for temperature measurements during the course of a treatment.

Of particular interest is the development of vacuum tubes capable of producing even shorter radiations than those used in therapy at present. The radiation from these oscillators is of the order of centimeters instead of meters, and such radiation has more pronounced optical properties than the radiation of the short wave field. This 1 to 100 cm. wavelength radiation may be focused<sup>26</sup> and directed along tubes.<sup>27</sup> These properties would seem to indicate that it would be particularly valuable in that the beam could be directed to a desired region. It would be of interest to know the absorption coefficients of this radiation and the extent of their dependence on wavelength and type of tissue. The newer tubes being developed are of the Magnetron type<sup>28</sup> or have resulted from newer designing of the more conventional negative grid tube.<sup>29</sup> It may be that many of the older problems and controversies that have marked the development and final utilization of long wave diathermy and short wave diathermy will reappear when these newer tubes are available for therapy and experiment.

16. Bachem, A.: The Resistance of Tissues for Various Electrical Currents. *Arch. Phys. Therapy* 11: 391 (Aug.) 1930. Hemingway, Allan, and McLendon, J. F.: The High Frequency Resistance of Human Tissue. *Am. J. Physiol.* 102: 56 (Oct.) 1932.

17. Schereschewsky, J. W.: Heating Effect of Very High Frequency Condenser Fields on Organic Fluids and Tissues. *Pub. Health Rep.* 48: 844 (July 21) 1933.

18. McLennan, J. C., and Burton, A. C.: Selective Heating of Short Radio Waves and Its Application to Electrotherapy. *Canad. J. Res.* 5: 550 (Nov.) 1931.

19. Bachem, A.: Selective Heat Production by Ultra Short (Hertzian) Waves. *Arch. Phys. Therapy* 16: 645 (Nov.) 1935.

20. Coulter, J. S., and Osborne, S. L.: Wavelengths in the Heating of Human Tissues by Short Wave Diathermy. *J. A. M. A.* 110: 639 (Feb. 26) 1938.

21. Schliephake, Erwin: Tiefenwirkungen im Organismus durch kurz elektrische Wellen. *Ztschr. f. d. ges. exper. Med.* 66: 212, 1929.

22. Mortimer, Bernard: Experimental Hyperthermia Induced by High Frequency Current. *Radiology* 16: 205 (May) 1931.

23. Binger, C. A. L., and Christie, R. V.: General and Local Heat Developed in Living Animal Body by Passage of High Frequency Currents. *Proc. Soc. Exper. Biol. & Med.* 24: 677 (April) 1927.

24. Mortimer, Bernard: Experimental Hyperthermia Induced by High Frequency Current. *Radiology* 16: 205 (May) 1931.

25. Coulter, J. S., and Osborne, S. L.: Short Wave Diathermy in Heating of Human Tissues. *Arch. Phys. Therapy* 17: 679 (Nov.) 1936; footnote 20.

26. Williams, N. H.: Production and Absorption of Electromagnetic Waves from 3 Cm. to 6 Mm. in Length. *J. App. Phys.* 8: 655 (Oct.) 1937.

27. Southworth, G. C.: New Experimental Methods Applicable to Ultra Short Waves. *J. App. Phys.* 8: 660 (Oct.) 1937.

28. Kilgore, G. R.: Magnetron as a High Frequency Generator. *J. App. Phys.* 8: 666 (Oct.) 1937. Schereschewsky, J.

29. Samuel, A. L.: Extending the Frequency Range of the Negative Grid Tube. *J. App. Phys.* 8: 677 (Oct.) 1937.

**HOGAN ADVANCE MODEL BREVATHERM,  
MODEL #8640, ACCEPTABLE**

Manufacturer: McIntosh Electrical Corporation, 233 North California Avenue, Chicago.

The Hogan Advance Model Brevatherm, Model #8640, is a portable short wave diathermy unit. It may be used for medical diathermy and for minor surgery. It is available with a mobile walnut or ivory finished cabinet, Model #8645. Standard accessories include one set of pad and one of cuff electrodes.



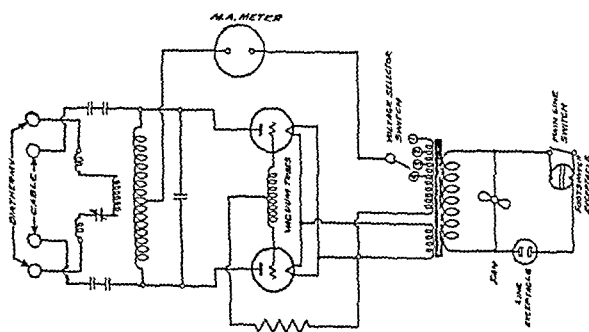
Hogan Advance Model Brevatherm, Model #8640.

Optional accessories consist of inductance cable and electrosurgical instruments.

The vacuum tubes in a tuned plate, tuned grid, push-pull oscillator circuit generate high frequency energy at a wavelength of approximately 12 meters. The output circuit for the cuff and pad electrodes is inductively coupled and the circuit for the cable is capacitatively coupled to the plate circuits of the oscillator.

The firm claims that the unit has an output of 240 watts as measured by a lamp load, photoelectric cell and wattmeter at a voltage of 116.5. The Council's investigator confirmed these claims. Transformer temperature rise and the temperature rise at various levels within the cabinet after a two hour run at full load were within the limits of safety prescribed by the Council.

The firm submitted thirteen tests, performed by a reliable investigator, as evidence of the unit's ability to produce heat deep in human tissues. The deep muscle temperatures were taken at a depth of about two inches, that is, the full length of the needle was inserted when the size of the leg permitted it. In other cases, the needle was inserted to the bone. A Leeds



Schematic Diagram of Circuit

Northrup Potentiometer was used as well as hypodermic needle thermocouples, in taking the temperatures. All determinations were run first on the right leg, then on the left. In all determinations the time interval between two successive tests on the same leg was never less than one-half hour. The time of

*Averages for Seven Observations, Cuff Technic*

Deep Muscle		Subcutaneous		Skin	
Initial	Final	Initial	Final	Initial	Final
98.1	106.2	94.3	102.7	87.9	92.3

*Averages for Six Observations, Coil Technic*

Deep Muscle		Subcutaneous		Skin	
Initial	Final	Initial	Final	Initial	Final
98.7	104.9	93.5	103.5	91.8	94.0

application was twenty minutes for each treatment. Room temperature ranged from 75 to 83 F. and the humidity varied from 62 to 70 per cent during the test periods.

Seven tests were made in which the cuff technic was used. The thigh was covered with three thicknesses of flannel and one of toweling, topped with a five-eighths inch strip of felt. The distance between cuffs was from 7 to 9 inches.

Six tests were carried out with the cable technic. A towel was first wrapped around the thigh single thickness and one-half inch felt strips were inserted between the coil and the towel.

The unit was investigated for the Council in a reliable clinic, where it was used for several months for general clinical application. It was reported a satisfactory unit.

In view of the foregoing report, the Council on Physical Therapy voted to accept the Hogan Advance Model Brevatherm, Model #8640, for inclusion in its list of accepted devices.

## Council on Foods

### ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION AND WILL BE LISTED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED.

FRANKLIN C. BING, Secretary.

### BAKER'S MODIFIED MILK, POWDERED AND LIQUID FORMS

Manufacturer.—Baker Laboratories, Cleveland.

**Description.**—Powdered form: A spray-dried homogenized mixture of evaporated skimmed milk, whole milk, lactose, coconut oil, beef fat, dextrose, cod liver oil and gelatin with added wheat germ extract and iron and ammonium citrates, U. S. P.

Evaporated liquid form: An evaporated homogenized mixture of evaporated skimmed milk, whole milk, lactose, coconut oil, beef fat, dextrose, cod liver oil and gelatin with added wheat germ extract and iron and ammonium citrates, U. S. P.

**Manufacture.**—Powdered form: The milk used is produced by tuberculin tested herds from an accredited area inspected by representatives of the Chicago Board of Health and is regularly inspected at the factory for quality and sanitation. Formula proportions of lactose, dextrose, coconut oil, beef fat, gelatin, cod liver oil, wheat germ extract and iron and ammonium citrates, U. S. P., are added to definite amounts of evaporated skimmed milk and whole milk. The mixture is pasteurized, homogenized, spray dried, packed into cans and hermetically sealed.

Evaporated liquid form: The milk used is the same as for Baker's Modified Milk, Powdered Form. Formula proportions of lactose, dextrose, coconut oil, beef fat, gelatin, cod liver oil, wheat germ extract and iron and ammonium citrates, U. S. P., are added to definite amounts of evaporated skimmed milk and whole milk. The mixture is pasteurized, homogenized, evaporated to a standard total solids content, filled into cans, sealed and heat processed.

**Analysis** (submitted by manufacturer).—Powdered form: moisture 1.4%, total solids 98.6%, ash 2.9%, fat 24.8%, protein (N  $\times$  6.38) 15.0%, carbohydrates (by difference) 55.9%. Liquid form: moisture 75.0%, total solids 25.0%, ash 0.8%, fat 6.4%, protein (N  $\times$  6.38) 3.8%, carbohydrates (by difference) 14.0%.

**Calories.**—Powdered form: 5.06 per gram; 144 per ounce. Liquid form: 1.28 per gram; 36 per ounce.

**Vitamin.**—Vitamin D: Powdered form, 3.9 U. S. P. units per gram; liquid form, 0.41 U. S. P. units per gram. Both powder and liquid forms supply not less than 400 U. S. P. units of vitamin D per quart, when diluted to "normal" strength as directed on the label.

### MRS. PALEY'S BABY FOOD—STRAINED EVAPORATED PRUNES

Manufacturer.—Paley-Sachs Food Company, Houston, Texas.

**Description.**—Cooked, sieved dried prunes.

**Manufacture.**—Dried prunes are washed, soaked for twelve hours, precooked in air-tight pressure cookers, automatically pitted, sieved, filled into glass jars, vacuum sealed and heat processed.

**Analysis** (submitted by manufacturer).—Moisture 68.3%, total solids 31.7%, ash 0.6%, fat (ether extract) 0.1%, protein (N  $\times$  6.25) 1.0%, reducing sugars as dextrose 17.1%, sucrose 0.6%, crude fiber 0.6%, total carbohydrates other than crude fiber (by difference) 29.4%, calcium (Ca) 0.026%, phosphorus (P) 0.034%, iron (Fe) 0.002%.

**Calories.**—1.2 per gram; 34 per ounce.

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SATURDAY, DECEMBER 17, 1938

## MODE OF ACTION OF SULFANILAMIDE

Apparently sulfanilamide possesses a specific chemotherapeutic effect on the beta-hemolytic streptococcus; it is of low toxicity, is easily administered, is quickly absorbed and is more effective in vivo than in vitro. The results obtained in the treatment of puerperal sepsis (Colebrook and Kenny) and in hemolytic streptococcus meningitis (Long and Bliss) are sufficiently dramatic to warrant the enthusiasm aroused by this new chemotherapeutic agent. Its administration in man is associated with definite though not necessarily unavoidable or serious hazards. In a recent communication, Long and Bliss<sup>1</sup> analyze toxic manifestations which have occurred during the course of treatment with sulfanilamide in 335 cases at the Johns Hopkins Hospital. The most common toxic effects manifested were dizziness, headache, a loss of ability to concentrate, anorexia, nausea and, in some instances, vomiting. Cyanosis of varying degrees was almost constant. This is said by some observers to be due to sulf-hemoglobinemia, by others to methemoglobinemia. Clinical acidosis as evidenced by combination of hypernoia and a lowered carbon dioxide combining power has been noted in 3 per cent of the cases. Jaundice occurred in only one case. Dermatitis occurred in 1 per cent and was apparently associated in one case with photosensitivity of the skin. Simple fever has been the most common toxic reaction noted (6 per cent). An early febrile response was likewise noted in all cases in which dermatitis, acidosis, acute hemolytic anemia or agranulocytosis developed. Anemias of the hemolytic type have occurred quite commonly and in 3 per cent of the cases were of the severe type characterized by a rapid fall in the red blood cell count in the hemoglobin, leukocytosis, reticulocytosis, bilirubinemia, urobilinuria and, in certain instances, porphyrinuria. Other authors have reported cases of agranulocytosis with occasional fatal results. Thus the most serious toxic manifestations are those associated with the blood

or hematopoietic system. The mechanism of this type of anemia is not clearly understood, but it would seem to be the result of an idiosyncrasy toward the drug.

Thus in sulfanilamide we have a potent chemotherapeutic agent for combating certain types of invasive bacterial disease. The precise mechanisms of its action on bacteria, as well as its toxic effects, have not been clearly elucidated. Progress is to be anticipated from the experimental studies rather than from the empirical observations of the clinic. A more or less scientific basis for the therapy of sulfanilamide was made possible through the experimental studies of Marshall and his co-workers.<sup>2</sup> They have developed a simple biochemical method for the quantitative demonstration of sulfanilamide in blood and in urine and have pointed out the importance of determining the concentration of the drug in the blood of patients undergoing treatment. Following a single oral dose, the drug is absorbed in about four hours. It is almost entirely excreted in the urine. By repeated dosage of the drug at intervals of four hours an equilibrium can be established between ingestion and elimination and the drug maintained at a definite concentration in the blood and tissues. These observations have been of the greatest importance in establishing a rational basis for therapy in infected human beings. Lockwood<sup>3</sup> demonstrated that the concentration of the drug in the amount of 10 mg. per hundred cubic centimeters of whole blood prevented the multiplication of young virulent streptococci in test tube experiments. Lockwood and his colleagues<sup>4</sup> similarly conclude in this issue of THE JOURNAL that the striking effect of sulfanilamide is a depression of the invasive properties of the organism. The optimum level for treatment in severe cases seems to lie between 5 and 10 mg. per hundred cubic centimeters of blood. Colebrook and his co-workers found sulfanilamide to be bactericidal against hemolytic streptococci in vitro and to a lesser degree in vivo. They did not, however, fail to observe the discrepancy between the striking therapeutic results obtained and the limited bactericidal effect in vitro. They concluded that the effect was the result of the combined bactericidal action of the blood plus that of the body tissues of the animal. Mellon, Cross and Cooper<sup>5</sup> found in their experiments that both sulfanilamide and its derivatives exhibited therapeutic effects in mice against hemolytic streptococcus infections. They found no indication that phagocytosis is a factor in the mechanism of the therapeutic action of these drugs. Likewise they failed to find qualitative changes in the character of the histologic response

1. Long, P. H., and Bliss, Eleanor A.: Toxic Manifestation of Sulfanilamide, *Ann. Surg.* **108**: 808 (Nov.) 1938.

2. Marshall, E. K.; Emerson, Kendall, Jr., and Cutting, W. C.: Para-Aminobenzenesulfonamide, *J. A. M. A.* **108**: 953 (March 20) 1937.

3. Lockwood, J. S.: Observations on the Mode of Action of Sulfanilamide and Its Application to Surgical Infection, *Ann. Surg.* **108**: 801 (Nov.) 1938.

4. Lockwood, John S.; Coburn, Alvin F., and Stokinker, Herbert E.: Studies on the Mechanism of the Action of Sulfanilamide, this issue, p. 2259.

5. Mellon, R. R.; Cross, Paul, and Cooper, F. B.: Experimental Studies with Sulfanilamide and with Prontosil, *J. A. M. A.* **108**: 1859 (May 29) 1937.

to the hemolytic streptococcus as the result of the administration of sulfanilamide, Lockwood found that normal serum without leukocytes is just as effective *in vitro* as a vehicle for the action of sulfanilamide in inhibiting the growth of streptococci. Lockwood found that addition of peptone to the serum in his experiments diminished the ability of sulfanilamide to restrict or to retard the growth of streptococci. He therefore concluded that the drug interferes with the ability of virulent hemolytic streptococci to use serum protein as a food from which to obtain nitrogen.

Most observers agree that the addition of sulfanilamide to nutrient broth or human serum slows the rate of multiplication but does not lead to the destruction of beta-hemolytic streptococci. The action of the drug, however, is not completely explained by this bacteriostatic influence, since it was proved that it enhances the bactericidal powers of human blood in infected patients. Lyons<sup>6</sup> found that sulfanilamide rendered human virulent strains of hemolytic streptococci more susceptible to the bactericidal action of human blood and that this effect is reversible on withdrawal of the drug. He found that in certain types of sustained hemolytic streptococcus bacteremias it was necessary to add an antibacterial antibody to sulfanilamide in order to obtain a therapeutic effect. The effective therapy for this type of infection should consist of sulfanilamide and the intravenous injection of specific antibacterial antibody by the immunotransfusion technic. He concludes that sulfanilamide induces a physiochemical alteration in the antigenic structure of hemolytic streptococci which decreases the invasive capacity or virulence of the bacteria.

#### FORMATION OF MILK PROTEINS

The phenomenon of lactation is of perennial interest to the physiologist, biologic chemist and pediatrician. Not only is the period of preparation an illustration of fine endocrine coordination and balance but the actual production of milk presents an opportunity to study metabolism taking place at an unusually rapid rate. The turnover of materials incident to the elaboration of large quantities of milk may present astounding values. Some dairy cows have made records of 100 pounds of milk a day; this yield means a large consumption of feed and water. It means the annual loss by way of the mammary glands of some 150 pounds of ash, of 25 pounds of calcium, of ten times the organic matter contained in the cow's body and of more than 1,000 pounds of protein.

The product of the mammary gland for several days post partum is unusually rich in protein. This secretion, called colostrum, contains in the case of the cow about 17 per cent of protein, a large proportion of which is a globulin identical with serum globulin. Ord-

narily globulin accounts for a small part of the total protein of milk, so that this high concentration in colostrum is striking and suggestive. It has been shown that this protein, after having been consumed by the newborn calf, passes unchanged through the intestinal wall into the blood, thus providing serum globulin for the calf whose blood during early life is essentially devoid of this immunologically important constituent.

The origin of the milk proteins was early studied by Cary,<sup>1</sup> who reported a withdrawal of amino acids from the blood as it passed through the mammary gland. He concluded that the proteins of milk arose from these amino acids taken from the blood. An analysis of the blood of lactating women, however, did not show any deviation from the normal in the level of amino acids.<sup>2</sup> Other reports showed that the nonprotein nitrogenous constituents of milk and those of blood were similar in concentration, and later identical values for urea were found in these two body fluids. That the protein of the gland itself is not changed in quantity has recently been shown by Jackson and Gortner;<sup>3</sup> this cannot be seriously considered as a source of milk proteins. A reexamination of the quantitative relationship between the amino acids withdrawn by the mammary gland and the milk protein formed by this gland has shown that not more than from 30 to 40 per cent of the total milk protein can be accounted for by the amino acids removed from the blood if all the amino acids are changed to protein.<sup>4</sup> A more recent study has indicated other sources of the milk protein; on the basis of extensive comparisons of the analysis of arterial blood with that of mammary venous blood, Graham, Peterson and Houchin<sup>5</sup> have concluded that serum globulin is removed by the mammary glands during active secretion. Furthermore, unidentified nonprotein nitrogenous compounds as well as amino acids pass from the blood into the glands at this time. The conclusion warranted by the current evidence is that the constituents of the blood from which the milk proteins can be synthesized by the mammary glands are amino acids, serum globulin and certain nitrogenous compounds of unknown nature.

The process of elaboration of milk is accompanied by intense nitrogen metabolism of another sort, which may or may not be concerned with protein synthesis. The gland forms urea in the course of its activity, raising the concentration of this substance in the mammary venous blood over that in the arterial blood.<sup>6</sup> Nursing or milking accentuates the production of urea by the glands. Shaw and Petersen<sup>7</sup> have shown that the active glands contain arginase, whereas the quiescent glands

1. Cary, C. A.: *J. Biol. Chem.* **43**: 477 (Sept.) 1920.

2. Hardings, V. J., and Downs, C. E.: *J. Biol. Chem.* **84**: 335 (Oct.) 1929.

3. Jackson, S. M., and Gortner, R. A.: *J. Biol. Chem.* **123**: 719 (May) 1938.

4. Shaw, J. C., and Petersen, W. E.: *Proc. Soc. Exper. Biol. & Med.* **38**: 632 (June) 1938.

5. Graham, W. R., Jr.; Peterson, V. E.; Houchin, O. B., and Turner, C. W.: *J. Biol. Chem.* **122**: 275 (Jan.) 1938.

6. Graham, W. R., Jr.; Houchin, O. B., and Turner, C. W.: *J. Biol. Chem.* **120**: 29 (Aug.) 1937.

7. Shaw, J. C., and Petersen, W. E.: *Proc. Soc. Exper. Biol. & Med.* **38**: 631 (June) 1938.

6. Lyons, Champ, with the Technical Assistance of Mangiaracine, Anita: The Effect of Sulfanilamide upon Human Virulent Hemolytic Streptococci, *Ann. Surg.* **108**: 813 (Nov.) 1938.



do not. This enzyme forms urea from the amino acid arginine and doubtless accounts for some of the urea which the gland loses to the blood. Whether the urea mechanism is a device to remove extra amino acids or is involved in the production of milk protein remains to be determined. Certain it is that recent investigation of the metabolism of nitrogen incident to the production of milk has brought us nearer to an understanding of the synthesis of proteins by the mammary gland.

## Current Comment

### SALIVARY INFLUENCE ON GALVANISM

Much has been written indicating that the electrical potential differences between dissimilar metals may produce damage to the mouth when such metals are used in dental restorations. Solomon and his co-workers<sup>1</sup> have recently reported a series of ingenious experiments to determine whether differences of potential actually exist between dental metals when saliva is the electrolyte. While the initial currents with saliva as the electrolyte are greater than currents with an artificial saliva, the final values are lower, showing that some action other than polarization is occurring, namely film formation. They concluded therefore that electric current is not normally flowing in the mouth containing dissimilar metal restorations. Although they do not maintain that electrical action resulting in damage to the soft tissues cannot exist in a mouth, the so-called protective mechanisms must be removed in order to permit current to flow. These investigators contend that there is no connection between the current readings obtained by placing a meter between metallic restorations in the mouth and damage to tissue.

### GERMICIDAL ACTION OF PROSTATIC FLUID

The demonstration by Youmans and his colleagues<sup>1</sup> of Northwestern University that prostatic fluid contains a bactericidal substance more powerful than blood serum is a belated confirmation of a generally accepted theory of genito-urinary immunity. The Northwestern University bacteriologists obtained prostatic fluid aseptically from dogs by the Farrell-Lyman technic, pilocarpine being used as the secretory stimulant. They tested its germicidal action against such micro-organisms as *Bacillus coli*, *Staphylococcus aureus*, hemolytic streptococci, *Streptococcus viridans* and the gonococcus. When *Bacillus coli*, *Staphylococcus aureus* or hemolytic streptococci were added to the undiluted prostatic fluid they found that the number of viable micro-organisms was reduced fully 95 per cent by the end of two hours. Within four to twenty-four hours all mixtures became sterile. This germicidal action was more rapid and complete than that of the blood serum of the same donors. Tests with the gonococcus showed a somewhat

slower rate of bacteriolysis, but all gonococcus mixtures became sterile by the end of twenty-four hours. The bactericidal power of canine prostatic fluid is but slightly reduced by dilution even with as much as twenty volumes of distilled water. The germicidal power, however, is reduced 50 per cent by heating the fluid to 55 C. for thirty minutes and is completely destroyed at 60 C. for thirty minutes. The bactericidal substance in prostatic fluid, therefore, is not identical with the lysozyme of tears or saliva, which resists heating to 75 C. for thirty minutes. Since the prostatic fluid will not activate hemolytic amboceptor it contains no demonstrable serum complement. Nor is the action of the germicidal factor increased by the addition of complement. Whether or not prostatic bacteriolysin is bound or inhibited in the presence of whole blood or pus has not yet been determined.

### SULFANILAMIDE AND BACTERIOSTASIS

In a recent report on the mechanism of action of sulfanilamide on bacterial infections, Osgood and Powell<sup>1</sup> found that sulfanilamide in concentrations of 1:1,000 or less did not inactivate in vitro significant amounts of the hemotoxins of the beta hemolytic streptococcus, hemolytic *Staphylococcus aureus*, *Clostridium oedematis-maligni*, *Clostridium tetani* or *Bacillus perfringens*. Neither did sulfanilamide therapy significantly affect the course of intoxication in guinea pigs injected with as little as 1 minimal lethal dose of diphtheric or tetanus toxin. The results of these experiments, therefore, fail to support, although they do not disprove, the earlier experiments with cultures of human bone marrow reported by the senior author indicating that sulfanilamide in some manner interferes with the production of the toxins responsible for the virulence of the organism and for its resistance to small amounts of bacteriocidins. Macgrath and Vollum<sup>2</sup> have recently investigated the bacteriostatic properties of three sulfanilamide derivatives using *Staphylococcus viridans* and *Staphylococcus aureus*, examined by the slide method of Wright, modified by Fleming. This technic was also used in cases of *Neisseria gonorrhoeae* and *Neisseria meningitidis*. All three derivatives apparently inhibited the growth of *Streptococcus viridans* in a dilution of 1:2,000 in the presence of defibrinated human blood but none of them were effective in the absence of leukocytes. None exhibited any bacteriostatic effects on *Staphylococcus aureus*; all three retarded the growth of *Neisseria gonorrhoeae* and *Neisseria meningitidis*. The bacteriostatic effect was dependent on the presence of leukocytes, which was in agreement with the observations previously reported by Fleming. The consensus at present is therefore that sulfanilamide and some of its derivatives exert a bacteriostatic effect in different degrees depending on the type of organism and the nature of the derivative but that the presence of leukocytes and probably some other factors are necessary for effective action.

1. Osgood, E. E., and Powell, H. M.: Failure of Sulfanilamide to Inactivate Preformed Hemotoxins, Diphtheric Toxin or Tetanic Toxin, *Proc. Soc. Exper. Biol. & Med.* **30**: 37 (Oct.) 1938.

2. Macgrath, B. G., and Vollum, R. L.: The Bacteriostatic Effects of Sulphonamide-P, Soluseptazine, and M & B 693, *Brit. M. J.* **2**: 985 (Nov. 12) 1938.

1. Solomon, H. A.; Reinhard, M. C., and Goltz, Hilda Lee: Salivary Influence on Galvanism, *Dental Items of Interest* **60**: 1047 (Nov.) 1938.  
1. Youmans, Guy P.; Liebling, Joseph, and Lyman, R. W.: *J. Infect. Dis.* **63**: 117 (July-Aug.) 1938.

# ORGANIZATION SECTION

## AMERICAN MEDICAL ASSOCIATION STUDY OF MEDICAL CARE

### Sullivan County, Tennessee

Sullivan County, Tenn., with a population of about 51,000, is located in the northeastern part of the state. The gainfully employed persons are about equally divided in agriculture and industry. The two industrial centers, Kingsport and Bristol, have a population of approximately 12,000 each.

The forty-six physicians in active practice in the county are located so that no person is more than 7 miles from the nearest physician. There are twenty practicing dentists, ten private duty nurses and ten public health nurses. There are two nonprofit general hospitals with a total of 111 beds. During 1937 the average bed occupancy was 41 per cent. Daily rates range from \$2.50 to \$6. In addition to two clinics operated by the hospitals there are five clinics maintained by the health departments and eight by welfare and relief agencies. Of the fifteen clinics, three provide general medical and surgical services and two are dental clinics. The rest provide limited special services but as a group they offer all types of medical and dental services.

#### *Record for One Week of Free Medical Services Furnished by Physicians*

1. Number of forms received.....	9
General practice.....	4
Surgery.....	2
Internal medicine.....	1
Eye, ear, nose and throat.....	2
2. Total number of persons who received any form of medical services in home or office.....	820
3. Total number of persons who were served without charge.....	141
4. Total number of persons referred to some other source for free medical care.....	23
5. Free surgical operations.....	13

The hospital provided 21,653 days of hospital care. Of this total, free patients received 2,716 days. In determining a patient's ability to pay, the hospital investigates his financial status and checks with the relief agency to see whether the patient is entitled to governmental aid.

Medical care for the indigents is provided by the Welfare Department, Salvation Army, Community Chest, Red Cross and Parrish Vance Foundation. These various organizations make their own investigations in determining the indigence of a person. If a person is found to be unable to pay for necessary medical care he is provided with free medical services at the various clinics. In addition to this public health nurses made 17,240 visits to patients at no charge, and the pharmacists provided 1,195 free prescriptions. The board of education provides free examinations and medical treatment for public school children.

Physicians and dentists reported that during 1937 there were thirty-two instances in which persons could not obtain medical care and the reasons given were listed as follows:

1. Lack of first class hospital.
2. Inability of patient to pay.
3. Refusal of physicians to take maternity cases in which antepartum care has not been given.
4. Refusal of patient to take advantage of services available.
5. Lack of free hospital service.

The welfare and relief agencies stated, however, that there were no cases of persons needing medical care who were not provided with the necessary services.

The amount of free medical care furnished by physicians may be estimated from the accompanying report, which is a summary of the data obtained from Form 1F.

Physicians in private practice through the health department and welfare agencies performed preventive medical services. Of the total number of children who entered school for the first time in 1937, 75 per cent were successfully vaccinated against smallpox.

In Kingsport and Bristol the larger business organizations provide industrial health services to their employees. The business men's clubs of these two cities are helpful in providing medical care, eye examinations and glasses when needed and food to needy children. In some cases these medical services are obtained for adults as well as for children.

The following comments and suggestions accompanied the county medical society summary sheet:

#### SUGGESTIONS FOR SUPPLYING MEDICAL NEEDS

##### Comments:

1. For fifteen years ample medical services have been available for all who applied.
2. Any lack of medical care in this community is due to failure of patients to avail themselves of the existent facilities.
3. A large group of diseases are nutritional rather than medical problems.
4. Many people who cannot afford adequate medical care will not go to a free clinic because of the 'stigma' attached to so doing.
5. There is a need for more adequate medical service to the indigent.

##### Suggestions:

1. Some free hospital beds for the indigent should be provided.
2. Complete care of cases should be relegated to the general practitioners. All clinic work, care of the indigent, and so on, should be done by physicians paid minimum fees for their service by relief and health agencies.
3. The most important needs in this locality are:
  - (a) Free choice of physician.
  - (b) Staff organization to improve hospital service.
  - (c) Hospitalization for very low income groups.
  - (d) A more efficient system of eliminating from charity those who are able to pay at least a small fee.
  - (e) More and better outpatient clinics.
  - (f) Organized follow-up clinics.
  - (g) Education of the public with regard to the value of medical attention early in an illness.

The county medical society makes the following conclusions and recommendations based on the experience of its members in making this study:

#### CONCLUSIONS AND RECOMMENDATIONS

It is our opinion, drawn from this study, that the medical care of the indigent is a community problem and an economic burden that has been borne too long by the physicians. The most equitable distribution of the costs of such care should be through tax support, and that cost should include anything

necessary for the care of the medically indigent person who is ill or injured, be it hospitalization, nursing or anything else that would make up an efficient medical regimen for that individual.

We advocate the free choice of physicians for the care of the medically indigent, and payment of those physicians for services rendered through the local governing unit. We have no desire to pass upon indigence because we feel that, while we have considerable information about certain families, owing to the nature of our profession, yet declaring a person medically indigent is the work of people trained for that purpose.

We disapprove of the employment of county or city physicians for the care of the poor, at least as far as it applies or is applied in Sullivan County. We find that no investigation is made of the indigent, but those who have been on the indigent roll for some time call the city or county physician to take care of their injuries or illnesses.

Owing to the past subsidization of our county health work by the Commonwealth Fund, we have a county health unit that is probably not only second to none in the state but ranks with the best of the country. It is exceptionally well housed in a building erected by the Commonwealth Fund.

The medical care of the prisoners at the county jail cannot be accomplished efficiently under the crowded, poor sanitary conditions existing in that institution. The same applies with regard to the medical care of people housed at the poor farm. The work in these two institutions is done under the supervision of county physicians who are inadequately paid for inadequate service. They have no facilities with which to do good work, and we cannot be proud of it.

The hospital service plan at Kingsport has the approval of the American Hospital Association and is working out very nicely. The hospital facilities in both Kingsport and Bristol are excellent; but this also, as far as housing and equipment are concerned, is due to subsidies by an outside agency, the Commonwealth Fund.

There is no sanatorium care provided for the patients with tuberculosis in East Tennessee. The facilities for the care of the insane are on a par with that which is happening in a large percentage of the states of the Union, in that a commitment to the state hospital automatically turns the patient over to the

sheriff, and the insane person is lodged in jail until he can be transported to an overcrowded state institution.

As already stated, we do not wish to pass upon indigence, but we wish it to be well done; and it was found during the depression of the early thirties that as a general rule counties did not have an efficient poor relief organization. We would therefore recommend that the federal government be requested by the American Medical Association to cooperate through the state government with county authorities, in subsidy funds and poor relief organization policy. Under this plan, both state and county, in order to qualify for such subsidy from the federal government, had to arrange for a businesslike efficient investigation and purchasing system in their relief work. This system, with a personnel properly selected by local county officials, was efficient. We know that the people who were doing that relief work in this county during the depression years did a good, conscientious, nonpolitical job.

The medical care of the indigent should be under the supervision of, and should be controlled solely by, physicians. The indigent person should have a free choice of physician from the list of the physicians in the county or group of counties who are willing to do this work at fees agreed on between the governing board of the county and the county medical society.

Bills for services rendered would be audited by a committee of physicians appointed by the county, and this committee should be composed of men who are willing to disagree and openly criticize any physician who attempted to impose on the system and make his relief work a "racket."

We feel definitely that there is going to be more socialization of medicine and that unless the American Medical Association and the Tennessee State Medical Association plan to meet the needs of the group who possibly cannot secure medical care and who are the group referred to by the Interdepartmental Committee in Washington as one third of the population, a system of state medicine will be crammed down our throats, and we shall have no alternative but to accept it.

We submit this plan as one that we believe will meet the need of the times and take away from the complete state medicine advocates their only definite evidence of the lack of distribution of medical care.

## GRADUATE MEDICAL EDUCATION IN MISSOURI

### Report of Recent Progress

At the last annual meeting of the Missouri State Medical Association, the Committee on Postgraduate Course recommended to the house of delegates that a correlating committee be formed of chairmen of the various state society committees concerned with professional and lay education.<sup>1</sup> October 13 the Postgraduate Correlating Committee was effected, with Dr. C. H. Neilson, who has been active in arranging postgraduate courses for several years, as chairman of the newly formed correlating committee and representatives from the committees on cancer, conservation of eyesight, fractures, health and public instruction, maternal welfare, medical economics, mental health, publication, physical therapy and the control of syphilis. Dr. John W. Williams, assistant health commissioner, also attended this meeting.

In the future the educational activities of these committees of the state association will be reviewed by the correlating committee, thus avoiding duplication of effort and insuring a well planned, comprehensive and continuous program of professional and lay instruction. Particular stress is to be given to the recording and publication of attendance at both scientific and lay meetings.

1. Association's Postgraduate and Health Education Activities Correlated, *J. Missouri M. A.* 35:454 (Nov.) 1938.

The newly formed correlating committee will strive to demonstrate to the public that individual practicing physicians are being thoroughly instructed and informed on the recent advances in medical science and practice under the present system of individual care. The plan of professional and lay education on preventive medicine of the Indiana State Medical Association, approved by the House of Delegates of the American Medical Association at the San Francisco session, forms the principles on which the Missouri association's postgraduate correlating committee will function. These are:

1. The selection of a specific disease or health problem of major importance for discussion in the state association's journal and in each county medical society. For each successive month, beginning in December, the following subjects have been chosen: pneumonia, highway accidents, syphilis, maternal and infant care and diphtheria. It is suggested that each component society select speakers from its own membership, whenever possible, to discuss current topics. Articles published in the journal should be of considerable assistance. Smaller county societies might arrange to meet jointly when circumstances permit.

2. Continued cooperation with the state board of health in the statewide program of lectures in obstetrics and pediatrics is strongly urged. Likewise, in the discussions of syphilis, the profession should be completely informed of the board's plan for the control and treatment of this disease.

3. The correlating committee does not propose to interfere with the activities of individual committees. As in the past,

the office of the state association will continue to be the clearing house for all committee activity. The number of physicians attending scientific sessions and the lay interest in health programs is to be reported routinely by the secretary of each component society to state association's office.

4. It has become a policy for the speaker designated for professional audiences to address lay groups as well when so requested by the local society.

5. Publicity on preventive health educational activities will be directed by the postgraduate committee in cooperation with the state association's office and component societies. Members of the committee on postgraduate course "believe that through such correlated activity we can successfully demonstrate to the public that individual practitioners of medicine are being thoroughly instructed and informed on the latest methods of medical progress. . . ."

## OFFICIAL NOTES

### WITNESSES BEFORE THE SPECIAL GRAND JURY IN WASHINGTON

The following additional witnesses are reported to have appeared before the Special Grand Jury in Washington, D. C.: Dr. John E. Rueth and Dr. Adam L. Curtin, both of Milwaukee.

### RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company, entitled "Your Health," began Wednesday October 19 and will run consecutively for thirty-six weeks. The program is broadcast each Wednesday over the blue network of the National Broadcasting Company at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).<sup>1</sup>

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived

1. Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.

from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

December 21. Hidden Treasures in Foods.  
December 28. Good Milk, Good for You.  
January 4. Fool's Gold.

### SPECIAL BROADCAST ON INFANTILE PARALYSIS

The American Medical Association and the National Broadcasting Company, in cooperation with the National Foundation for Infantile Paralysis and the Committee for the Celebration of the President's Birthday, will broadcast a special program on infantile paralysis over the red network of the National Broadcasting Company December 19 at 11:30 p. m. to midnight, eastern standard time (10:30 central standard time, 9:30 mountain time and 8:30 Pacific time).

This will be a dramatized program, with music, along the same general lines as the regularly weekly programs in the Your Health series. The program will be conducted by Dr. W. W. Bauer and the principal speaker will be Dr. Morris Fishbein.

## WOMAN'S AUXILIARY

### Georgia

Dr. Grady N. Coker, president of the Medical Association of Georgia, spoke on "Our Problems" at a recent meeting of the auxiliary to the First District Medical Society. Dr. W. H. Myers, president-elect, spoke on "What Is Happening in the Practice of Medicine."

The auxiliary to the Third District Medical Society held a joint meeting with the society in Eastman recently. Speakers and their subjects were as follows: Mrs. Warren A. Coleman, president of the auxiliary to the Medical Association of Georgia, "Auxiliary Activities for 1938-1939"; Mrs. Eustance Allen, president-elect, "Organization"; Mrs. John Persall, "The Jane Todd Crawford Memorial," and Mrs. R. L. Cater, "Research in the Romance of Medicine."

### Iowa

The auxiliary to the Dallas-Guthrie Medical Society met at Panora October 20. Mrs. Dean W. Harman, president of the Iowa Auxiliary, gave the four auxiliary objectives for the year: 1. Extend aim of medical society to all organizations interested in health. 2. Assist in entertainment work at state meetings. 3. Promote friendship among families of physicians. 4. Continue to cooperate with medical societies in all tasks for which they ask our help.

### New Jersey

The auxiliary to the Atlantic County Medical Society met October 4 at the Ambassador Hotel, Atlantic City. Dr. Hilton S. Read was speaker. Mrs. Andrew Smith, president, announced the essay contest sponsored by the auxiliary for children of the seventh and eighth grades of the public schools of Atlantic County.

The auxiliary to the Bergen County Medical Society met at Teaneck October 11. At the request of the society, three needy physicians will be assisted from the philanthropic fund of the auxiliary.

The auxiliary to the Hudson County Medical Society met in Jersey City October 3. Mr. David Armstrong, professor of English in the Emerson High School, Union City, reviewed the Biography of Madame Curie, written by her daughter.

The auxiliary to the Middlesex County Medical Society met at Perth Amboy October 27. Mrs. Don Epler, president of the state auxiliary, was guest of honor. Dr. Rita Finkler of Newark, director of the biologic laboratory at the endocrine clinic, Beth Israel Hospital, Newark, spoke on "Recent Advances in Endocrinology."

Dr. Sigurd Johnsen of Passaic spoke on "Socialized Medicine" at the meeting of the auxiliary to the Passaic County Medical Society October 10.

### Oklahoma

The auxiliary to the Woodward County Medical Society, comprising the five counties of Beaver, Harper, Ellis, Dewey and Woodward, hold joint meetings alternate months. October 15, Dr. Louis H. Ritzhaupt spoke on "Socialized Medicine." The project for the year is to organize a speakers' bureau and to furnish programs on public health for lay groups.

The auxiliary to the Pontotoc County Medical Society met in Ada October 19. Mrs. C. F. Needham gave a talk on "Public Relations." The auxiliary is cooperating with the American Association of University Women in federal nursery work and during the past month supplied cod liver oil, food-stuffs and toilet articles for thirty needy children.

The auxiliary to the Tulsa County Medical Society held a tea in Tulsa October 4 with ninety-two members present. Copies of "On the Witness Stand," a booklet on socialized medicine, was distributed.

### Tennessee

The Woman's Auxiliary to the Nashville Academy of Medicine and the Davidson County Medical Society gave a dinner October 24 in honor of Dr. Harrison H. Shoulders, Nashville, Speaker of the House of Delegates of the American Medical Association, and Mrs. Shoulders.

### Wisconsin

The auxiliary to the Dane County Medical Society met in Madison October 12. Mr. J. G. Crownhart, secretary of the Wisconsin Medical Society, spoke on "Looking at Sickness Care in Europe." Mr. Crownhart was speaker also at the meeting of the Milwaukee County auxiliary October 14 on the subject "Current Medical Problems."

The auxiliary to the Sheboygan County Medical Society assisted the society and the Crippled Children's Division of the Department of Public Instruction at the orthopedic clinic held in Sheboygan September 26.

## MEDICAL ECONOMIC ABSTRACTS

### DIPHTHERIA PREVENTION IN ENGLAND

A vivid comparison of the preventive measures taken against diphtheria and the results of such measures in the United States and Great Britain is found in the following extract from the Annual Report of the Chief Medical Officer of the Ministry of Health for the year 1937 "On the State of the Public Health," London, 1938, pages 53-55:

In 1937, 61,339 cases of diphtheria were notified as compared with 57,795 in 1936 and 65,084 in 1935. The fatal cases numbered 2,963, giving the fatality rate of 4.8 per cent as compared with 5.3 per cent and 5.4 per cent in 1936 and 1935 respectively. In diphtheria we appear to have reached a position of stability so far as incidence is concerned within the limits of what may be regarded as normal fluctuation, and it is doubtful whether any marked diminution of incidence can be expected by procedure along the old lines of "notification, removal and disinfection."

Approximately 90 per cent of cases of diphtheria occur under the age of 15 years. By that time the great majority of individuals have become immunized by the subclinical infection. This is a measure of the amount of natural subinfection which is constantly taking place. The acquisition of immunity by natural means postulates a diphtheritic environment. It is a lengthy process and is obtained at the expense of a number of clinical cases, and possibly of deaths, whereas artificial immunity if carefully conducted by experts is without these risks and can be acquired in as many months as the natural process takes years. A clear indication would appear to be to induce a wider adoption of artificial immunization, such as has been practiced in certain cities of the United States of America and in Canada with extraordinary success.

#### RESULTS OF IMMUNIZATION IN NORTH AMERICA

In New York immunization against diphtheria has been a practice for about twenty years. An intensive campaign began in 1929 and by the middle of 1935 more than 1,110,000 children under the age of 15 years were immunized in addition to those protected in previous years.

Before 1929 comparatively little attention has been paid to children of preschool age on whom, as previously pointed out,<sup>1</sup> the maximum incidence and fatality falls, but in 1929 in New York special attention was paid to the children, and the total number of immunized persons rose from 212,000 in 1929 to 1,114,325 in 1935. Of this last number 650,000 were under the age of 6 years and it is estimated that between 65 and 70 per cent of them had been protected. There resulted a reduction in diphtheria incidence from 8,548 cases in 1929 to 1,143 in 1936. That is to say, the incidence in the latter year was about one-eighth what it had been in the former. During the same period the deaths diminished from 463 to thirty-five. The later figures represent a reduction in the diphtheria death rate in the age period 1 to 15 from 27.4 to 2.1 per hundred thousand. The corresponding figures for England and Wales are 32.8 and 31.8 respectively.

In Montreal, among a population of 657,000 in 1928 when immunization was commenced, there were 1,632 cases and 157 deaths from diphtheria. Both incidence and mortality fell *pari passu* with immunization until in 1935 there were 183 cases

and twenty-one deaths, approximately one tenth of the figures recorded in 1927. As in New York, a particular effort to secure the protection of young children was made and it was calculated that by the end of 1935 over 50 per cent of the child population under the age of 12 was immunized. Among other smaller cities of Canada showing an almost similar record are Toronto (650,000), Hamilton (150,000), where there has been no case of diphtheria notified since 1933 and no death since 1930, Brantford (31,382) and St. Catharines, Ont. (27,000). Of Brantford it is said that no child has suffered from diphtheria there since 1930, and from that date no resident of St. Catharines has died from diphtheria.<sup>2</sup>

These results have been achieved only by intensive propaganda on the part of local authorities, assisted in some degree by insurance interests, and it is, of course, necessary to ensure that the immune population thus obtained is not unduly diluted with nonimmunes in the persons of recently born infants, for, as Dr. Graham Forbes<sup>3</sup> recently observed, the further success of immunization must be dependent on the respective campaigns being continuous and unremitting in order to keep the protection rate at least equal to one-half the number of births each year.

It is now six years since the minister issued his memorandum on "The Production of Artificial Immunity against Diphtheria" and drew the attention of local authorities to the advantages of this process, at the same time expressing the opinion that the public should be made aware of them, and, where practicable, parents and guardians of children over 1 year of age should be offered the necessary facilities for protection. A survey of the annual reports for 1936 of medical officers of health, the last complete available information, shows that local authorities generally are well acquainted with the memorandum and continuous if slow progress is being made, particularly in some of the larger provincial cities, although none of them have yet succeeded in immunizing the 50 to 60 per cent of the child population which is necessary before the incidence of the disease is affected. Chester, with an estimated number of 45 per cent, is probably the best immunized town in the country; then follow in close order Birmingham, Walsall, Worcester, Leeds, Manchester and Chatham, all of which are in the neighborhood of from 35 to 40 per cent. Other towns with more than 30 per cent are Wood Green, Wakefield, Salford, Blackburn, Swindon, Cardiff and Acton. London (all the metropolitan boroughs combined) appears very low in the list, with an estimated number of 5.3 per cent of her child population immunized.

It may be said in conclusion that artificial immunization against diphtheria as done in the United States and Canada has been attended by extraordinarily good results. This work has to be persisted in over a long period of time before the necessary number of immunes are obtained to affect the incidence of the disease. It is unfortunate that the exact technique, preparation of vaccine and method of administration are still matters of medical controversy. It is probable that the lack of a general standard has militated against the more general adoption of antidiphtheritic immunization in this country. It is a form of preventive treatment which in the future may succeed in eradicating diphtheria from our midst and thus save countless lives. It is desirable that medical practitioners should

2. Fitzgerald, J. G.; Fraser, D. T.; McKinnon, N. E., and Ross, Mary A.: *Lancet* 1: 391 (Feb. 12) 1938.  
3. Forbes, J. Graham: *Brit. M. J.* 2: 1209 (Dec. 18) 1937.

1. Annual Report of Chief Medical Officer of Ministry of Health for 1934, p. 26.

acquaint themselves with the minister's memorandum and, if possible, gain practical experience at a clinic where immunization is done, in order that they may be familiar with the method when called on to apply it. The medical officer of health of the county or county borough concerned is usually able to make the necessary arrangements for medical practitioners to acquire experience in the technic employed in Schick testing and immunization, and applications should be made to him.

## INFANT MORTALITY IN GERMANY

When so much is being said about comparative infant mortality statistics, it is worth while to look at some of the facts. Germany has had sickness insurance longer than any other nation in the world. In the *Deutsches Aerzteblatt* (68:681 [Oct. 1] 1938) Hans Klepp reports on "The Struggle Against Infant Mortality" and gives a table showing the course of infant mortality during the present century, from which the following figures are taken:

Death Rate per Thousand Live Births During the First Year

Year	Male	Female	Both
1901.....	223	190	207
1905.....	222	188	205
1910.....	176	147	162
1913.....	164	137	151
1914.....	177	149	164
1918.....	172	143	158
1919.....	158	131	145
1923.....	144	118	131
1928.....	99	79	89
1929.....	107	86	97
1932.....	87	71	79
1933.....	85	68	77
1935.....	77	60	69

The Bureau of the Census, Department of Commerce, has also issued a summary of the changes in infant mortality in the registration area since 1915 (Vital Statistics—Special Reports 5:47 [March 1] 1938). Every state that is in any way comparable as to climate and racial uniformity with Germany shows a lower infant mortality rate. Of eleven northern states that have been in the registration area since 1920, the range of the infant death rate per thousand in 1935 is between 41.2 for Oregon and 53.9 for New Hampshire.

## PWA HOSPITAL CONSTRUCTION

According to a report on "Allotments for Hospital Construction" by the Federal Emergency Administration of Public Works, Projects Division, Research Section, Dec. 2, 1936, and supplemental report as of Jan. 15, 1938, the total estimated cost of constructing and equipping 1,161 hospital buildings was \$194,567,038. Nine hundred and twenty-two of these buildings had reached a point where it was possible to determine the number of additional beds provided, which amounted to 51,207.

## DISCOVERING THE OBVIOUS

The United States Department of Agriculture reports on part of "a nation-wide study of how much money the American family makes and how it is spent." This proves once more that low income families consult dentists less frequently than doctors and that visits to the oculist usually are omitted entirely. It demonstrates again that persons with an annual income of less than \$500 spend less for medical care than higher income families. It was also discovered that "a majority of families with very low incomes did not have periodic physical examinations by a doctor." The report does not state whether those with higher incomes had such periodic physical examinations. What this report and all others like it fail to tell is that almost all that is being done about this condition is due to the action of organized medicine and individual physicians, assisted by relief appropriations in some cases. Neither, of course, are any comparisons made to indicate whether the medical care received by members of the same income levels in other countries is as good as or better than the care received in the United States.

## INCOMES OF PHYSICIANS

A survey of the income of some types of professional workers by the United States Bureau of Foreign and Domestic Commerce is summarized in the *Monthly Labor Review* (47:1114 [Nov.] 1938).

As table 1 shows, the number of practitioners in the sample was too small to make the estimates given reliable as measures

TABLE 1.—Net Income of Independent Professional Practitioners, 1929-1936

Profession	Average Net Income							
	1929	1930	1931	1932	1933	1934	1935	1936
Medical								
All practitioners.....	\$3,298	\$4,687	\$4,065	\$3,145	\$2,909	\$3,310	\$3,629	\$4,143
General practitioners...	4,701	4,084	3,603	2,790	2,615	2,964	3,231	3,673
Specialists.....	8,341	7,734	6,402	4,964	4,397	5,112	5,636	6,521
Legal.....	16,001	*	*	4,088	3,786	3,692	3,885	4,320
	15,561	*	*	*	3,273	*	*	3,725
Accounting								
C. P. A.....	5,749	*	*	*	*	4,012	4,291	4,626
Non-C. P. A.....	3,303	*	*	*	*	2,226	2,463	2,910
Dentistry.....	*	*	*	2,778	2,465	2,780	*	*
Percentages of 1929								
Medical								
All practitioners.....	100	88.5	76.7	50.4	51.0	62.5	68.5	78.2
General practitioners...	100	86.9	76.6	50.3	53.6	62.8	65.7	78.1
Specialists.....	100	93.0	77.0	59.7	52.9	61.5	67.8	78.4
Legal.....	1100	*	*	61.9	57.4	55.9	58.9	65.4
	1100	*	*	*	58.9	*	*	67.0
Accounting								
C. P. A.....	100	*	*	*	*	69.8	74.6	80.5
Non-C. P. A.....	100	*	*	*	*	67.4	74.6	88.1
Dentistry.....	*	*	*	*	*	*	*	*
Number of Practitioners in Sample								
Medical								
All practitioners.....	753	752	791	850	912	1,033	1,048	1,037
General practitioners...	593	592	622	669	724	835	828	834
Specialists.....	160	160	169	181	188	218	220	223
Legal.....	1557	*	*	\$683.8	734	777	787	\$784.5
	1706	*	*	*	944	*	*	1,157
Accounting								
C. P. A.....	695	*	*	*	*	896	916	961
Non-C. P. A.....	45	*	*	*	*	57	57	61
Dentistry.....	*	*	*	1,007	1,007	1,007	*	*

\* Information not obtained for these years.

† Averages based on the questions asked by the Department of Commerce.

‡ Averages obtained from supplementary questions included for the American Bar Association.

§ Fractions indicate part of year participation in legal firms.

TABLE 2.—Net Income and Percentage Distribution of Medical and Legal Independent Practitioners, by Years of Experience, 1936

Years of Experience	Medical			Legal		
	Persons in Sample		Average Net Income	Persons in Sample		Average Net Income
	Number	Per Cent		Number	Per Cent	
Total.....	1,378	100.0	.....	1,090	100.0	.....
1 year.....	16	1.1	\$ 925	30	2.7	\$1,059
2 years.....	40	3.6	1,839	53	4.9	1,121
3 years.....	79	5.7	2,747	48	4.4	1,630
4 years.....	50	3.6	3,060	50	5.4	1,779
5 years.....	45	3.3	3,553	60	5.5	2,047
6 years.....	45	3.3	3,622	54	4.9	2,176
7 years.....	30	2.2	3,693	42	3.9	2,375
1 to 2 years.....	65	4.7	1,614	83	7.6	1,699
3 to 7 years.....	249	18.1	3,229	263	24.1	1,990
8 to 17 years.....	302	21.9	4,030	326	29.9	3,629
18 to 27 years.....	278	20.2	4,683	207	19.0	4,893
28 to 37 years.....	323	23.4	3,717	139	12.7	4,664
38 to 47 years.....	142	10.3	2,325	33	3.0	4,016
48 to 52 years.....	17	1.2	1,600	13	1.2	2,591
Over 52 years.....	2	0.2	678	6	0.6	1,245

of the income of all physicians. Nevertheless, the agreement of the figures given with other investigations lends some measure of confidence regarding the accuracy of the results.

An effort is also made to determine the income by years of experience. Here again the number in some years is so small as to indicate a large "probable error," which should be kept in mind in any use that may be made of these statistics.



## Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

### ARIZONA

**Annual Registration Due January 1.**—Every person practicing medicine, surgery or osteopathy in Arizona is required by law to pay annually on or before January 1, to the board of medical examiners, a renewal license fee of \$3. Any licentiate who does not renew his license as required is to be penalized \$1 for each day that he practices without a renewal license, not to exceed \$50. The board of medical examiners is to revoke the license of any licentiate who fails to renew his license for three successive years.

### ARKANSAS

**Annual Reregistration Due January 1.**—Every licentiate of the Arkansas Eclectic Medical Examining Board must register annually with the secretary of the board between January 1 and the last day in February and pay a fee, if a resident of Arkansas, of \$2, and, if a nonresident, of \$4. The failure of a licentiate to pay the required fee by March 1 automatically suspends his right to practice while delinquent. If he fails for three successive years to pay the required fee his license is to be canceled, and thereafter he will be reinstated only on such a showing to the board of moral character and professional qualifications as would entitle the applicant to the issuance of an original license and the payment of the same fee as is required for the issuance of an original license.

### CALIFORNIA

**Annual Registration Due January 1.**—Every practitioner of medicine and surgery holding a license to practice in California is required by law to register annually, on or before January 1, with the secretary-treasurer of the board of medical examiners and at that time to pay a fee of \$2. Failure to pay the required fee within sixty days after January 1 works a revocation of a license and thereafter a license may be reissued only after application and the payment of a \$10 penalty.

**Four Persons Indicted for Treating Alcoholism.**—Four persons were indicted by the grand jury November 19 on charges by the state board of medical examiners that a South American arrow poison had been used in the treatment of alcoholic addicts, according to the newspapers. Under indictment were Thomas F. H. Huston, proprietor of the "Samaritan Treatment," an establishment offering to cure alcoholism, and his assistant, John A. Stevens, neither of whom has a medical degree; and two nurses, Ruth Nielsen and Juanita Butcher. It was stated that more than 200 complaints have been received by the state board against the treatment. The newspapers reported that two investigators for the board found that curare was used in the treatment.

**Positions Open for Physicians.**—The state personnel board announces several positions open for physicians, the examinations to be held January 5. There are vacancies for physician and internist, junior physician, physician (eye, ear, nose and throat) and physician and surgeon. Applications by nonresidents must be filed by December 26. Examinations will be held in San Francisco, Los Angeles, San Diego, Sacramento, Fresno, New York, Chicago, St. Paul, Madison, Wis., Washington, D. C., Denver, Portland, Ore., Seattle, Dallas, Texas, Columbus, Lansing, Mich., Jacksonville, Fla., Baltimore, Boston, and Phoenix, Ariz., and such other cities outside the state of California as the number and location of candidates may warrant. Information may be obtained from the state personnel board, 1025 P Street, Sacramento.

### CONNECTICUT

**Personal.**—Dr. Julius Lane Wilson, assistant clinical professor of medicine, Yale University School of Medicine, New Haven, has been appointed associate professor of medicine at Tulane University of Louisiana School of Medicine, New Orleans.—Dr. Russell V. Fuldner, chief, division of crippled children, state department of health, Hartford, has resigned to accept a residency in orthopedic surgery at Massachusetts General Hospital, Boston.

**Annual Registration Due During January.**—Every practitioner of medicine and surgery holding a license to practice in Connecticut is required by law to register during January with the state department of health and at that time to pay a fee of \$2. Licentiatees who have retired from active practice or who live out of the state must register annually but need not pay a fee. A practitioner failing to register is liable to a fine of not more than \$5.

**Exhibition of Rare Medical Volumes.**—Yale University School of Medicine, New Haven, recently sponsored an exhibition of books commemorating the two hundredth anniversary of the death of Hermann Boerhaave, professor of botany, chemistry and clinical medicine at the University of Leyden. Boerhaave was born in 1668 and died in 1738. Lent by Dr. John F. Fulton, Sterling professor of physiology at Yale, the books included a first edition of Boerhaave's "Institutiones Medicae," published in 1708, which for the first time established physiology as an academic discipline in the medical curriculum, according to *Science*, and was written to give his students a background of knowledge of normal function; in the work he introduces the term "physiology" in its modern connotation.

### FLORIDA

**Annual Registration Due January 1.**—Every practitioner of medicine and surgery holding a license to practice in Florida is required by law to register annually on or before January 1 with the secretary of the state board of health and at that time to pay a fee of \$1. A licentiate failing to register annually is liable to a fine of not more than \$50.

**Personal.**—Dr. Terry Bird, Tavares, has been appointed in charge of the newly created Lake County health unit.—Dr. James Maxey Dell Sr., superintendent of the Florida Farm Colony, was named mayor-commissioner of Gainesville recently, succeeding R. B. Livingston.—Dr. Lauren M. Sompayrac, Jacksonville, was recently awarded the Robert L. Schermer Cup by the local junior chamber of commerce in recognition of his "meritorious leadership" during the past six months. Dr. Sompayrac graduated from the University of Pennsylvania School of Medicine, Philadelphia, in 1935.

### ILLINOIS

**Society News.**—Dr. Norbert C. Barwasser, Moline, discussed the management of common skin diseases before the Whiteside County Medical Society, Sterling, November 21.—The Peoria City Medical Society was addressed November 1 by Lewis Gerber, Ph.D., on "Recent Advances in Clinical Chemistry" and Dr. Hugh E. Cooper on "Fractures of the Shaft of the Femur."—Dr. Edmund F. Foley, Chicago, discussed "Jaundice: Its Clinical Significance" before the Adams County Medical Society in Quincy November 14.—Dr. Fred W. Bailey, St. Louis, discussed "Nonpenetrating Intra-Abdominal Injuries" before the Madison County Medical Society in Alton November 4.

### Chicago

**Lectures on Psychoanalysis.**—A group of introductory lectures on psychoanalysis began at the University of Illinois College of Medicine November 30 under the auspices of the Institute for Psychoanalysis. Dr. Franz Alexander, director of the institute, is making a systematic presentation of medical psychoanalysis. Sixteen weekly lectures make up the course, which carries a fee of \$10.

**Society News.**—The Chicago Laryngological and Otological Society was addressed November 7 by Drs. Ellison L. Ross on "Experiences with a Vital Stain in Otolaryngeal Tissues"; Frank E. Simpson, "Intrinsic Carcinoma of the Larynx—A New Instrument Modeled After the Jackson Bronchoscope for the Intralaryngeal Application of Radon," and Hans Brunner, "Inflammatory Diseases of Meninges and Brain of Pharyngeal Origin."—Dr. Frederick A. Collier, Ann Arbor, Mich., discussed "Hypochloremia Associated with Surgical Diseases" before the Chicago Surgical Society November 4; Drs. Loyal Davis and John Martin, "Surgical Aspects of Paratrigebral Lesions," and Geza DeTakats, "Observations of Congenital Megacolon."

### KENTUCKY

**Date of Dr. J. N. McCormack's Death.**—In the news item concerning the new building of the Kentucky State Board of Health and the Kentucky State Medical Association recently dedicated as a memorial to Dr. Joseph N. McCormack, published in THE JOURNAL December 10, page 2219, the date of Dr. McCormack's death should have been May 4, 1922, instead of Aug. 4, 1922.

## LOUISIANA

**Annual Renewal Due January 1.**—Every practitioner of medicine and surgery holding a certificate to practice in Louisiana is required by law to have his certificate renewed annually on or before January 1 by the secretary-treasurer of the state board of medical examiners and at that time to pay a fee of \$2. The board may by unanimous vote revoke any certificate not renewed.

**Society News.**—At a meeting of the Orleans Parish Medical Society in New Orleans November 14 Drs. Richard S. Crichtow spoke on "Treatment of Headache with Theelin"; Upton W. Giles, "The Historical Development and Modern Application of Artificial Fever," and George Gordon McHardy III, "Peritoneoscopy."—Dr. Edward Garland Walls was recently elected president of the New Orleans Eye, Ear, Nose and Throat Club and Dr. William B. Clark secretary-treasurer.

## MASSACHUSETTS

**Infectious Encephalitis Made a Reportable Disease.**—At a meeting of the public health council in Boston October 11 it was voted to substitute the term "infectious encephalitis" for "encephalitis lethargica" on the list of reportable diseases in Massachusetts. The change was made because of the belief that the term "encephalitis lethargica" is not broad enough to include all cases of encephalitis that are of possible danger to public health. The new terminology will exclude encephalitis caused by chemicals and degenerative changes. On the other hand, "infectious encephalitis" should include cases of encephalitis which appear to result from an apparent communicable disease or vaccination.

**Dr. Christian to Retire from Brigham Hospital.**—Dr. Henry A. Christian, Hersey professor of the theory and practice of physic, Harvard Medical School, Boston, will retire next September as physician-in-chief of Peter Bent Brigham Hospital, a position he has held since the hospital was completed in 1912. A portrait of Dr. Christian was presented to the hospital corporation October 13 at a gathering of 350 friends and pupils. Dr. Christian received his medical degree at Johns Hopkins University School of Medicine, Baltimore, in 1900. He was pathologist at the Boston City Hospital from 1900 to 1905 and at the Children's Hospital, Boston, 1903 to 1905. During the latter period he taught pathology at the Harvard Medical School, changing in 1905 to the theory and practice of physic, becoming Hersey professor in this subject in 1908. He was dean of the medical school from 1908 to 1912 and physician-in-chief to Carney Hospital from 1907 to 1912. He was secretary of the Section on Pathology and Physiology of the American Medical Association from 1903 to 1905, chairman of the section from 1905 to 1907 and of the Section on Practice of Medicine, 1916-1917. He was resident chairman of the division of medical sciences of the National Research Council, 1919-1920; president of the American Society for Clinical Investigation in 1919 and the Association of American Physicians in 1935. He is editor for the Oxford University Press of Oxford Medicine and Oxford Monographs and has contributed extensively to medical literature. On his sixtieth birthday in 1936, Dr. Christian was presented with a volume of medical papers dedicated to him by his former students and colleagues.

## MINNESOTA

**Annual Registration Due During January.**—Every practitioner of medicine and surgery holding a license to practice in Minnesota is required by law to register annually during January with the secretary of the board of medical examiners and at that time to pay a fee of \$2. A licentiate who practices without renewing his license is guilty of a misdemeanor and is liable to prosecution.

## MISSOURI

**Pilgrimage to Beaumont's Grave.**—The St. Louis Medical Society conducted its annual birthday pilgrimage to the grave of William Beaumont November 21. Rev. Harry B. Crimmins, S.J., president of St. Louis University, where Beaumont was the first professor of surgery, was the speaker.

**Society News.**—At a meeting of the Boone County Medical Society in Columbia October 4 the speakers included Dr. William J. Stewart, Columbia, on "The Smith-Petersen Nail in Treatment of Fractures of the Femur."—At a meeting of the Buchanan County Medical Society in St. Joseph November 2 Dr. Thomas L. Howden discussed "Common Types of Neuroses."—The Southeast Missouri Medical

Society held its sixty-second annual meeting at Poplar Bluff October 11-12. Dr. George W. Vinyard, Jackson, the only living charter member of the society, was present. Dr. Bernard J. Macauley, Poplar Bluff, was chosen president and Cape Girardeau was selected as the place of the next annual meeting in October.

## NEW JERSEY

**Scarlet Fever Isolation Period Reduced.**—The state department of health recently amended the state sanitary code to reduce the minimum period of isolation of cases of scarlet fever. The amendment, which went into effect October 1, changes the quarantine from thirty to twenty-one days.

**Second Councilor District Meeting.**—At a meeting of the Second Councilor District of the Medical Society of New Jersey in Jersey City December 15 the speakers were Drs. Morris Fishbein, Chicago, Editor of THE JOURNAL, on "American Medicine and the National Health Program"; William J. Carrington, Atlantic City, president of the state society, "Medicine in the News," and Hilton S. Read, Atlantic City, "Voluntary Medical Costs Insurance."

**Annual Health Meeting.**—The sixty-fourth annual meeting of the New Jersey Health and Sanitary Association was held at Asbury Park November 18-19. There were sessions on cancer, mental hygiene and social hygiene, motion picture showings, a microscopic exhibit of common parasites in New Jersey and an exhibit of publicity material. Among the speakers were Drs. William G. Herrman, Asbury Park, chairman of the cancer control committee of the Medical Society of New Jersey, on "The Cancer Situation in New Jersey"; Clarence C. Little, Sc.D., Bar Harbor, Maine, managing director, American Society for the Control of Cancer, "The Public and Cancer Control"; Haven Emerson, New York, "Signs of the Times in Public Health," and Mr. Homer Calver, director of health exhibits, New York World's Fair, "Health Exhibits, World's Fair and Otherwise."

## NEW YORK

**Annual Graduate Lectures.**—The eleventh annual series of graduate lectures sponsored by the Medical Society of the State of New York in Rochester was presented during October. The following addresses were given:

Dr. Samuel J. Kopetzky, New York, October 3, Recent Developments in the Treatment of Paranasal Sinusitis and Mastoiditis, Including the Use of Roentgenology and Chemotherapy.

Dr. Foster Kennedy, New York, The Organic Background of Mind.

Dr. Samuel W. Clausen, Rochester, Latest Developments in Vitamins.

Dr. Henry H. Ritter, New York, Treatment of Burns and Hand Infections.

Dr. Henry Rawle Geyelin, New York, Diabetic Coma.

**Annual Registration Due January 1.**—Every practitioner of medicine and surgery in New York is required by law to apply annually, on or before January 1, to the secretary of the board of medical examiners for a certificate of registration, on application forms furnished by him, and to pay at that time a fee of \$2. The law authorizes the secretary of the board to permit secretaries of duly incorporated medical societies to act as his representatives, to receive and transmit to him such applications and fees. Practitioners are liable to severe penalties for failing to register and for continuing in practice thereafter.

### New York City

**Another Orchestra.**—The Doctors' Musical Society of Brooklyn was recently organized and an orchestra is in process of formation. Dr. Harry Tevel Zankel, 614 Eastern Parkway, Brooklyn, is secretary.

**Brickner Lecture.**—The eighth Walter M. Brickner Lecture was given at the Hospital for Joint Diseases November 17 by Dr. Charles A. Elsberg. His subject was the orthopedic and neurologic significance of back pain.

**Bronx Society to Honor Dr. Van Etten.**—The Bronx County Medical Society will celebrate its twenty-fifth anniversary Jan. 7, 1939, with a dinner dance at which Dr. Nathan B. Van Etten will be the guest of honor. Dr. Van Etten, for several years medical director of Morrisania Hospital, was the first president of the Bronx County society. For three years Dr. Van Etten was Speaker of the House of Delegates of the American Medical Association, having retired at the San Francisco session in June. In 1925 he was president of the Medical Society of the State of New York.

**Society News.**—Drs. John G. Kidd and Fred W. Stewart, New York, addressed the New York Pathological Society November 18 on "Immunologic Studies with Virus-Induced and Transplantable Growths of Rabbits" and "Use

of the Aspiration Biopsy in Diagnosis of Tumors" respectively. Dr. Richard E. Shope of the Rockefeller Institute for Medical Research, Princeton, N. J., delivered the Middleton Goldsmith Lecture December 7 on "Complex Infections."—At a meeting of the New York Diabetic Association with the section of medicine of the New York Academy of Medicine December 20 the speakers will be Drs. Herman Lande, on "Present Status of Protamine Zinc Insulin Therapy"; Edward Tolstoi, "Protamine Zinc Insulin: A Metabolic Study of Two Severe Cases of Diabetes with Comments on Criteria for Treatment," and Henry Rawle Geyelin, "Management of Diabetic Acidosis and Its Accompanying Medical Shock."—Dr. William Osler Abbott, Philadelphia, will address the New York Roentgen Society December 19 on "The Role of Small Intestinal Intubation in the Treatment and Diagnosis of Intestinal Obstruction."

### NORTH DAKOTA

**Annual Registration Due January 1.**—Every practitioner of medicine and surgery holding a license to practice in North Dakota is required by law to register annually on or before January 1, with the secretary-treasurer of the board of medical examiners and at that time to pay a fee of \$5 if a resident of North Dakota or \$2 if a nonresident. A practitioner may not lawfully practice if he has not registered. If he does so his license may be revoked and can be reinstated on the payment of unpaid fees and \$0.50 for each month of default.

### OHIO

**Western Reserve Selected for Cancer Training Center.**—The National Cancer Institute has chosen Western Reserve University School of Medicine as one of the centers for training of physicians in the diagnosis and treatment of cancer. Appointments are filled at present, but, as vacancies may arise, those interested should apply promptly to the Surgeon General, U. S. Public Health Service, Washington, D. C. Appointments are for two years, with eight months each of pathology, radiology and surgery. Applicants must have had at least three years of hospital training, one of which may have been a rotating internship; at least two years must have been in surgical experience. Not more than one trainee can be accepted at present, but the number may later be increased to three, according to the announcement. Trainees will be paid by the National Cancer Institute on a per diem basis, out of which they will be expected to pay all the necessary expenses, including tuition, if any is charged by the institution which accepts them for training. Stipends for training will range from a per diem allowance of from \$5 to \$10, depending on training, experience and other considerations. Further information and application blanks may be obtained on written request to the Surgeon General at Washington or from Dr. John H. Lazzari, Secretary of the Cancer Training at Western Reserve University, Republic Building, Cleveland, Ohio.

### OREGON

**Society News.**—Dr. Herbert Van H. Thatcher, Portland, addressed the Central Willamette Medical Society, Newport, recently on "Injuries of the Hand."—Dr. Warren G. Bishop addressed the Jackson County Medical Society, Medford, recently on common colds.—Dr. Arthur J. McLean addressed the Multnomah County Medical Society, Portland, October 19 on "The Adequate Neurological Examination," and Dr. Homer P. Rush gave a demonstration of electrocardiography. The speaker October 5 was Dr. Robert W. Langley, Los Angeles, on "Heart Sounds: A Clinical Experiment in Sound Photography." The society held its first hobby show September 24 with sixty physicians as exhibitors; more than 1,000 persons attended.

### PENNSYLVANIA

**Annual Registration Due January 1.**—Every practitioner of medicine and surgery holding a license to practice in Pennsylvania is required by law to register annually on or before January 1 with the board of medical education and licensure in the department of public instruction and to pay a fee of \$1 or such fee as may be fixed by the department of public instruction. A practitioner who fails to register and who continues to practice is liable to a fine of from \$10 to \$100.

**Society News.**—Dr. Albert D. Ruedemann, Cleveland, addressed the Cambria County Medical Society, Johnstown, November 10, on "A Clinical Survey of 100 Cases of Headache."—Drs. Arthur Carlton Ernestine and Robert S. Dinsmore, Cleveland, addressed the Lycoming County Medical

Society, Williamsport, at its annual clinic meeting November 11 on "Use of Drugs in Heart Disease" and "Problems in Thyroid Surgery" respectively.—Drs. Thomas B. Herron, Monessen, and Albert S. Sickman, Lock No. Four, addressed the Washington County Medical Society at Lock No. Four November 9 on "The Ruptured Appendix" and "Immediate Operation of Compound Fractures" respectively.—Dr. Edward S. Dillon, Philadelphia, addressed the Delaware County Medical Society, Chester, November 10 on "Diabetic Coma."—Dr. Charles F. Geschickter, Baltimore, addressed the Northampton County Medical Society November 17 on "Neoplasms of the Mammary Gland."

### RHODE ISLAND

**Subject for Fiske Fund Essay.**—The trustees of the Fiske Fund, administered by the Rhode Island Medical Society, have chosen the following subject for the prize essay of 1939: "Cesarean Section—Indications and Contraindications for the Various Types of Operations." Competitors must forward to the secretary, Dr. Wilfred Pickles, 184 Waterman Street, Providence, copies of their dissertations before May 1, 1939. Each must be identified by a motto and accompanied by an envelop bearing the same motto on the outside and the name and address of the sender within.

### SOUTH CAROLINA

**Dr. Jervey Honored.**—The Greenville County Medical Society held a dinner in honor of Dr. James W. Jervey, Greenville, then president of the Southern Medical Association, November 7 in Greenville. The speakers were Drs. William Weston, Columbia; Robert Wilson, Charleston; Frank H. McLeod and William S. Fewell, Greenville. At the society's meeting Drs. Edwin A. Merritt, Washington, D. C., and Kenneth M. Lynch, Charleston, spoke on "Carcinoma of the Cervix" and "The Evolution of Cancer Control and Knowledge" respectively.

**Society News.**—Dr. Addison G. Brenizer, Charlotte, N. C., addressed the Newberry County Medical Society, Newberry, November 10, on "The Evolution of Thyroidectomy." Other speakers were Drs. Austin T. Moore, on "Fractures—Some Fundamental Principles in Their Treatment"; Roger G. Doughty, "Head Injuries," and Lucius Emmett Madden, "Coronary Thrombosis"; all are of Columbia.—Dr. Rock Sleyster, Wauwatosa, Wis., President-Elect of the American Medical Association, addressed the Columbia Medical Society November 14 on "Medical Problems of the Day." Dr. George Bolling Lee, New York, addressed the society October 10, on "Chorio-Epithelioma" and Dr. James Heyward Gibbes, Columbia, on "Tick Paralysis as Indicative of Growing Menace from Ticks as Carriers of Disease."

### TEXAS

**Annual Registration Due January 1.**—Every practitioner of medicine and surgery holding a license to practice in Texas is required by law to register annually on or before January 1 with the state board of medical examiners and at that time to pay a fee of \$2. If a practitioner fails to renew his registration within sixty days after January 1 his license is suspended.

### WEST VIRGINIA

**Personal.**—Dr. Norman G. Angstadt, New Martinsville, has been appointed health officer of Wetzel County to succeed Dr. John B. Hozier, acting health officer during the past year.—Dr. William A. Bevacqua, Charleston, has been appointed health officer of Parkersburg and Wood County to succeed Dr. Arthur D. Knott, Parkersburg, resigned.—Dr. David B. Ealy, Moundsville, was elected to the state senate in the November election.

**Society News.**—Dr. Edward M. Livingston, New York, addressed the Kanawha Medical Society, Charleston, October 11, on "Abdominal Pain."—Dr. Wilbur E. Hoffman, Charleston, addressed the Monongalia County Medical Society, Morgantown, October 4, on "Ruptured Uterus."—Dr. Vernon L. Peterson, Charleston, was the speaker at a meeting of the Raleigh County Medical Society, Beckley, October 20, on silicosis.—The Wood and Kanawha county medical societies held a joint meeting October 20 at the Spencer State Hospital. Drs. Jacob J. Alpers and Mark Thumin of the hospital staff read papers on shock therapy of mental patients. Dr. George D. Johnson, superintendent of the hospital, entertained the visiting physicians and the state board of control at a dinner in the hospital dining room.

## GENERAL

**Outbreaks of Tularemia.**—Twelve deaths from tularemia have been reported in Illinois since the hunting season opened November 10; according to the newspapers of December 12. More than 250 cases have been reported. The sale and transportation of rabbits have been barred in East St. Louis, where twenty-six cases were reported within fifteen days. In Indiana fifty-five cases were reported in the first ten days of December, as compared with thirty-three cases during the entire month in 1937. Cases have been reported in Iowa and Ohio, although Illinois is said to be leading in prevalence.

**Symposium on Glycols.**—The pharmacy section of the American Association for the Advancement of Science will present a special session on glycols December 27 at the meeting in Richmond, Va. The speakers will be:

Frank C. Whitmore, Ph.D., State College, Pa., Chemistry of the Glycols.  
Herbert O. Calvery, Ph.D., chief pharmacologist, Food and Drug Administration, U. S. Department of Agriculture, Washington, D. C., Pharmacology of the Glycols.

Mr. H. B. McClure, Carbide and Carbon Chemicals Corporation, Industrial Application of the Glycols.

Andrew G. DuMez, Ph.D., Baltimore, Pharmaceutical Uses of the Glycols.

Discussion will be opened by Drs. Harvey B. Haag, Richmond, and Michael G. Mulinos, New York.

**Society News.**—The National Gastroenterological Association announces that it has taken an office with its official publication, the *Review of Gastroenterology*, at 1819 Broadway, New York.—The sixteenth annual meeting of the American Orthopsychiatric Association will be held in New York at the Hotel Commodore, Feb. 23-25, 1939. Dr. Norville C. LaMar, New York, is the secretary.—The Pacific Coast Surgical Association will hold its next annual session in San Francisco, Oakland and Del Monte, March 28-31, 1939. Dr. Harry Glenn Bell, University of California Hospital, San Francisco, is the secretary.—Dr. Jennings C. Litzenberg, Minneapolis, was chosen president-elect of the Central Association of Obstetricians and Gynecologists at its annual meeting in Minneapolis in October. Dr. Ralph A. Reis, Chicago, became president and Dr. Thomas B. Sellers, New Orleans, was elected vice president. Dr. William F. Mengert, Iowa City, was reelected secretary.

**Posthumous Award of Sedgwick Medal.**—The American Public Health Association at its meeting in Kansas City October 25-29 awarded its Sedgwick Medal posthumously to Dr. Wade Hampton Frost, professor of epidemiology at Johns Hopkins University School of Hygiene and Public Health, Baltimore, who died May 1. Dr. Frost served as dean of the Johns Hopkins school of hygiene from 1931 to 1934 and had been professor since 1921. He was associated with the U. S. Public Health Service from 1905 to 1929. During the World War he was director of the bureau of sanitary science of the American Red Cross. In a statement at the meeting in Kansas City Dr. Haven Emerson, New York, on behalf of the medal committee, said: "While his illuminating contributions in the fields of poliomyelitis, influenza, diphtheria and tuberculosis stand high among the classics of epidemiology, perhaps his planning, direction and guidance of the stream pollution laboratory at Cincinnati will prove to have been his most abundant legacy to the expanding fields of the theory and practice of public health."

**Southwestern Medical Association.**—The annual session of the Southwestern Medical Association was held in El Paso October 28-29 with headquarters at the Hotel Cortez. The guest speakers were:

Dr. Charles A. Bahn, New Orleans, Prevention of Blindness from the Standpoint of the General Practitioner; Practical Ophthalmic Advances for the General Physician.

Dr. Horton R. Casparis, Nashville, Public Health Aspects of Childhood Tuberculosis; Medical Aspects of Healthy Child Behavior; Allergy in Children.

Dr. George T. Caldwell, Dallas, Texas, Estimation of Kidney Function; Pathology of Vitamin Deficiencies.

Dr. Raymond W. McNealy, Chicago, Preoperative Management of the Jaundiced Patient; Dietary Deficiencies in Surgical Patients; Management of Blood Vessel Injuries and Their Sequelae.

Dr. Edward H. Rynearson, Rochester, Minn., Complications of Diabetes; Present Day Methods of Treating Goiter; Recent Advances in Endocrinology.

Dr. Curtice Rosser, Dallas, Texas, Diagnostic Criteria of Rectal Cancer; Rational Management of Hemorrhoids; Rational Management of Minor Anal Conditions.

Chauncey D. Leake, Ph.D., San Francisco, Antiseptic Agents; Epinephrine, Ephedrine and Their Derivatives; Art in Medicine.

Dr. Orville E. Egbert, El Paso, was chosen president-elect of the association and Dr. Howell S. Randolph, Phoenix, Ariz., was installed as president. Drs. Ralph W. Mendelson, Albuquerque, N. M., and Jesse D. Hamer, Phoenix, were elected vice presidents and Dr. Maurice P. S. Spearman, El Paso, Texas, is secretary.

**Foundation for Infantile Paralysis Extends Organization.**—A new plan of organization in county units was adopted by the National Foundation for Infantile Paralysis at a meeting of its trustees and officers in New York November 10. Permanent county chapters are to be organized as fast as possible after the campaign for funds, which will reach its climax on President Roosevelt's birthday, Jan. 30, 1939. In addition to the plan for field organization, the officials of the foundation decided that the funds raised this year will be divided on a 50-50 basis, half to be sent to the national committee and half to be retained in the counties where the money is raised. It is planned that county chapters will work closely with the national committee in helping victims of poliomyelitis, in disseminating knowledge of diagnosis and treatment and in emergencies in times of epidemics. Funds left in the counties will be held as trust funds for the account of the national foundation and will be administered under general rules and regulations laid down by the national foundation, according to the announcement, but within those limitations expenditures will be in the discretion of the local chapter or unit.

**Low Tuberculosis Mortality Rate.**—The National Tuberculosis Association, which opened its thirty-second annual sale of Christmas seals Thanksgiving Day, announces that the death rate from tuberculosis dropped from 55.5 per hundred thousand in 1936 to 53.5 in 1937, the lowest ever reported. The 1936 rate was the highest in ten years, an increase attributed to the cumulative effects of the depression. In 1936 71,239 persons died of tuberculosis and in 1937 the number



was 69,151. Fifteen states showed an increase over 1936, but this was more than balanced by decreases in thirty-two states. Michigan's rate remained the same and the District of Columbia showed a decrease. Among the states in which notable decreases were reported were: Arizona, 258.5 from 271.2 the previous year; Maine, 33.5 from 40.6; New Hampshire, 28 from 33.9; North Carolina, 54.8 from 60.8; Tennessee, 84.7 from 89.6, and Virginia, 59.4 from 64.2.

Wyoming reported a rate of 18.3, the lowest of any state, though it was an increase from 15 reported in 1936. The highest rates were in Arizona and New Mexico, with 258.5 and 113.3 respectively, followed by the District of Columbia with 94.9. Case finding activities increased in twenty-seven states, according to the report. Thirteen states and the District of Columbia exceeded the standard ratio of two new cases reported to each death in any year. The states were Connecticut, Idaho, Illinois, Maryland, Massachusetts, Michigan, Minnesota, Montana, New Jersey, New Mexico, New York, Oregon and Washington.

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## Government Services

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### Dr. McIntire Appointed Surgeon General of Navy

President Roosevelt announced November 29 the appointment of Dr. Ross T. McIntire, who for five years has been White House physician, as surgeon general of the U. S. Navy, with the rank of rear admiral. Dr. McIntire was first commissioned in the navy in 1917 and his rank was that of commander, although he was temporarily a captain at the time of his latest appointment. The President has not yet announced the appointment of the new White House physicians, of whom there will be two from now on, according to newspaper reports. Dr. McIntire was born in Salem, Ore., Aug. 11, 1888, graduated from the Willamette University Medical Department, Salem, in 1912 and was first commissioned in the medical corps of the navy April 4, 1917. Prior to assignment to duty as White House physician he was in charge of the eye, ear, nose and throat service at the Naval Hospital in Washington. As Surgeon General he succeeds Dr. Percival S. Rossiter, who retires from active service because of the age limit. In reaching the rank of rear admiral, Dr. McIntire, in service parlance, was jumped over the heads of thirty-four commanders and eighty-four captains. A native of Shepherdstown, W. Va., Dr. Rossiter has been a member of the medical corps of the U. S. Navy since 1903. He was a member of the U. S. Naval Mission to Brazil, 1922-1926; commanding officer of the Brooklyn Naval Hospital, 1929-1932, Washington, D. C., Naval Hospital, 1932-1933. In 1933 he became surgeon general. He graduated at the University of Maryland School of Medicine, Baltimore, in 1895.

## Foreign Letters

### LONDON

(From Our Regular Correspondent)

Nov. 19, 1938.

#### The Public Health

The report for 1937 of the chief medical officer of the Ministry of Health, which has just been published, shows that the birth rate was 14.9 per thousand living, a slight rise on 14.8 for 1936 and 0.5 above that for 1933, which was the lowest on record. The infant mortality was 58 per thousand births, against 59 for 1936, but one point higher than the exceptionally low figure of 57 in 1935. The five principal killing diseases remain the same as for many years and in the same order: (1) diseases of the heart and circulatory system, (2) malignant disease, (3) respiratory diseases, (4) diseases of the nervous system, (5) tuberculosis. But if the diseases are arranged to show the principal killing diseases in the years of working life from 15 to 65 years, tuberculosis takes the third place and diseases of the nervous system the fifth. There has been a decline in the incidence of lethargic encephalitis and scarlet fever but an increase in that of cerebrospinal fever, diphtheria, dysentery, influenzal pneumonia and acute poliomyelitis. The maternal mortality continues to fall, being 3.13 against 3.65, 3.94 and 4.41 in 1936, 1935 and 1934. Puerperal sepsis accounted for 0.94 per thousand, leaving 2.19 for other causes. There is evidence that fresh infection with syphilis is declining. There is no evidence that cancer is becoming less prevalent. More than half as many males were killed by injury as by all the infectious diseases taken together, and a large proportion of these violent deaths occurred on the roads. Statistical inquiry has revealed that there are accident-prone just as there are sickness-prone persons, i. e., persons for whose abnormal sickness rate no physical grounds can be assigned and malingering can be excluded. A great extension has been made of the scheme of graduate education for panel physicians, who it is intended will receive a free course every five years. Not only will the course be paid for but also traveling and subsistence costs and the cost of a locum tenens when one is necessary.

#### Rectal Ulceration Due to Cancer of Cervix

When new drugs are found valuable in treatment it is only later and gradually that their possible toxic effects become evident. The same statement holds true for radiotherapy, which has proved such an important advance in the treatment of cancer. It is only recently that it has been discovered that the radium treatment of cancer of the cervix uteri may produce chronic ulceration of the rectum. But little has been published on the subject, and the pathology of the condition has not been described. During the tenure of a research scholarship at the Christie Hospital and Holt Radium Institute, Manchester, Mr. T. F. Todd has had personal experience in thirty-four cases of chronic ulceration of the rectum in 800 cases of cancer of the cervix treated by radium. In a report to the North of England Obstetrical and Gynaecological Society he stated that this reaction was frequently overlooked and several cases were referred after previous radium treatment elsewhere for what was misdiagnosed as cancer of the rectum. The cases were of two types: 1. A lesion restricted to the anterior rectal wall, usually at the level of the cervix uteri, forming a mobile ulcerated mass from 3 to 5 cm. in diameter and resembling an operable carcinoma. 2. A rectal ulceration similarly situated, but accompanied by gross perirectal induration and formation of a hard fixed mass enveloping the rectum and anchoring it to the sacrum, resembling advanced inoperable cancer with extensive extrarectal spread. In its early stage the

rectal ulceration took the form of acute proctitis. The reaction might be due to overdosage from slipping of the radium applicators and their approximation to the rectum in the posterior fornix or to retroversion which allowed the intra-uterine applicator to project against the rectum. The main factor appeared to be obliteration of blood vessels from the high dosage.

The symptoms usually began after from six to nine months' treatment. They included tenesmus, melena and severe pain. Spontaneous healing was the rule, but stenosis of the rectum might occur and require colostomy. The incidence of the ulceration could be reduced by precautions to avoid misplacement of the vaginal applicators and overdosage and by nursing patients in the prone position. In four cases presacral neurectomy was done for the relief of pain and acceleration of healing. It was suggested that it might act as a prophylactic against massive perirectal fibrosis by producing vasodilatation.

#### Toxic Effects of Sedormid

Attention has recently been directed to the toxic effects of the hypnotic sold under the name of sedormid (allyl-isopropyl-acetyl-carbamide). A number of cases of purpura haemorrhagica have been recorded. In the *Lancet*, Miller and Rosenheim suggest that it is a dangerous drug. They report a case in which a woman physician aged 26 was given two tablets of sedormid nightly while convalescent after thyroidectomy. She found it an excellent hypnotic, but after six weeks' use a widespread purpuric rash appeared. Though the drug was stopped she became acutely ill and the purpura was complicated by severe epistaxis. Her blood films showed almost complete absence of platelets, and despite three transfusions the hemoglobin fell in ten days to less than 30 per cent. Two further transfusions were necessary before the platelet counts began to increase. Discussing two cases of severe thrombocytopenic purpura due to the use of sedormid for insomnia, in the *British Journal of Dermatology*, the editor (Dr. A. C. Roxburgh) states that he has seen two cases of eruption, not purpuric, due to this cause. Both patients were women between 60 and 70 years of age. In one there was a red circinate eruption on the neck, cheeks, upper part of the back, sternum and backs of the hands. In the other patient there was a red scaling patch measuring 1 by 1½ inches on the back of the forearm, raised about one-fourth inch. It took several weeks to disappear. In both patients the eruption ceased after the sedormid was stopped but it recurred in the first patient when she resumed the drug.

#### The British Heart Journal

With the beginning of the new year the British Medical Association will publish a quarterly journal devoted to disease of the heart and circulation under the title of the *British Heart Journal*. This journal, which is being published at the request of the Cardiac Society of Great Britain and Ireland, will be edited by the cardiologists Dr. Maurice Campbell and Dr. Evan Bedford. The *British Medical Journal* states that, as diseases of the heart and circulatory system are the first of the principal causes of death at all ages in this country, it is a matter of surprise that such a journal is not already in existence. This does not overlook *Heart*, which for many years was edited by Sir Thomas Lewis and held a unique position among the medical periodicals of the world—a position still maintained with change of title to *Clinical Science* but happily without any change of editor. The research in experimental medicine that is carried out by Sir Thomas Lewis and is reported in this journal is of supreme importance to medicine and represents a field that probably will be only incidentally surveyed in the *British Heart Journal*. The new periodical will deal with work more concerned with the everyday diagnosis and treatment of patients and so will be of immediate value to the practicing physician. The appeal will be to the cardiologist.

ogists, both at home and in other countries, but the journal is commended to all physicians "to whom the stethoscope of Laënnec has become the badge of their tribe." In form it will be similar to the other two special journals published by the *British Medical Association*. The subscription will be \$6 a year.

## PARIS

(From Our Regular Correspondent)

Nov. 19, 1938.

### Recovery from Meningococcic Meningitis After the Use of Sulfanilamide

At the October 14 meeting of the Société médicale des hôpitaux of Paris Dr. R. A. Marquezy and his associates reported two cases of meningitis due to the meningococcus in which recovery followed the administration of sulfanilamide alone. In all cases which have previously been reported, chemotherapy was preceded by serotherapy. The authors cited a study by Muraz, Chirle and Queguinier (*Presse médicale*, July 16, 1938) of 397 cases of meningococcic meningitis treated during an epidemic of the disease in French Nigeria. The mortality in forty-nine cases in which serum alone was given was 22.44 per cent; in twenty-three cases in which serum and sulfanilamide (by mouth) were given, 8.7 per cent; in thirty-nine cases in which sulfanilamide given by mouth was preceded by one intraspinal injection of the drug, 15.38 per cent; in ten cases in which sulfanilamide given by mouth was preceded by two intraspinal injections of the drug, no deaths, and in 271 cases in which sulfanilamide given by mouth was the only therapy, 10.7 per cent.

In both of the cases reported by Marquezy and his associates, only sulfanilamide was given. The first patient, a boy aged 16, was given 7 Gm. a day by mouth for the first seven days and gradually decreasing amounts during the next twelve days. In addition, an intraspinal injection of an 0.8 per cent solution was given daily for fifteen days, the average amount being 10 cc. The second patient, a man aged 25, was given sulfanilamide only by mouth. Intraspinal administration is preferable at the onset as it secures a concentrated solution of the drug in the spinal fluid at the earliest possible moment.

In the discussion Dr. Weill-Hallé reported an additional case with recovery, in which only sulfanilamide was employed. Dr. Marquezy stated that sulfanilamide had not been found to be of any value in a personally observed case of pneumococcic meningitis. Dr. Benda suggested the use of sulfanilamide-pyridine in such cases.

### French Otorhinolaryngologic Congress

The president of this year's meeting of the French Otorhinolaryngologic Congress, held in Paris October 24-26, was Dr. le Mée. The subject of the first report, by Drs. Collet and Mayoux of Lyons, was auricular tuberculosis. Although it is generally taught that from 5 to 10 per cent of the cases of chronic otitis media and mastoiditis are of tuberculous origin, the authors believe that this percentage is far too low, because in many cases the disease is not correctly diagnosed. Tuberculous otitis is at times observed clinically as an associated condition with pulmonary tuberculosis. Usually, however, the condition occurs independent of pulmonary localization. The clinical picture then differs considerably from that observed when it is an associated condition. Most commonly there is a history of an acute onset, resembling in every respect the clinical picture in cases of ordinary nontuberculous otitis. With children, tuberculous otitis should be thought of if there has been exposure to tuberculous adults, if the granulation tissue formed after a mastoid operation is flabby and pale and contains caseous particles, and if a fistula persists after mastoidectomy. In all such cases a search for underlying tuberculosis must be made with the aid of the guinea pig inoculation method. This had confirmed the clinical diagnosis in twenty-

two cases. The prognosis, unless pulmonary lesions exist, is far more favorable than is generally believed. The treatment is surgical followed by heliotherapy and actinotherapy. As to the pathogenesis, the authors were of the opinion that the infection was primary in the nasopharynx and involved the middle ear by way of the eustachian tube.

## TUMORS OF HYPOPHARYNX AND LARYNX

The subject of the second report, by Drs. Huët of Paris and Péri of Algiers, was roentgenologic exploration of tumors of the hypopharynx and larynx. The first objective in exposing films is to obtain profile views of the hypopharynx and larynx. The second objective is to secure anteroposterior views. The various technical methods to secure satisfactory exposures were described in detail. At the Paris Cancer Institute it has been found that 60 per cent of tumors of the hypopharynx originate in the piriform sinuses. Some are very radiosensitive and show but little tendency to extension, whereas others are very malignant. The remainder of this thorough review of the roentgenologic methods of diagnosis contained chapters on the search for endolaryngeal tumors and lesions of the cartilages.

## POLYPS OF LARYNX; MENINGITIS

Drs. Piquet and Boury of Lille reported four cases of malignant changes in polyps of the larynx; hence every papilloma should be regarded as a potential cancer. Dr. Leroux-Robert said that a polyp was a purely inflammatory lesion and must be distinguished from a papilloma. The latter was a precancerous condition, but this was not true of a polyp. This point of view was confirmed by Professor Lemaître of Paris.

Dr. Marcel Ombredanne of Paris reported three cases of streptococcic meningitis of otitic origin in which recovery had followed the use of a preparation similar to sulfanilamide. In only one of the three cases had the drug been employed exclusively, i. e., no operation performed. Those who took part in the discussion of this paper believed, however, that it is advisable always to operate and to give the drug as an adjuvant.

## BERLIN

(From Our Regular Correspondent)

Nov. 8, 1938.

### The Extent of Poliomyelitis in Germany

For several years a number of cases of epidemic poliomyelitis have been reported each summer from some part of the German reich. The locality affected varies from year to year. In general a year of severe epidemic is succeeded by several years during which the erstwhile stricken community remains more or less spared from the disease. An official survey just published by the national health bureau traces the incidence of the disease in Prussia since 1909 and in the entire reich since 1924. In 1909 a great wave of poliomyelitis occurred in Germany. Yet as soon thereafter as 1910 poliomyelitis had become a fairly rare disease. Not until 1926 did the morbidity rise again and in 1927 it attained a new peak with 2,840 cases. In 1928 the number of new cases again dropped to one third of the corresponding number for 1927. Thereafter the morbidity slowly increased from year to year until 1932. The latter year was marked by a severe epidemic (the most severe thus far, the cases numbering 3,869). In 1933 the number receded to one-third that of the previous year. Subsequently and down to date it has developed a gradual upward trend from one year to another. There were 2,256 cases reported in 1936 and 2,723 in 1937. According to these official statistics the 1938 figure will be higher than that for 1937.

In other countries also greatly increased incidences have been noted in recent years, particularly in the Scandinavian lands since 1934 and in Austria, Switzerland and Italy since 1936. At present an increased morbidity is reported from the Nether-



lands, whereas in the other foreign countries mentioned no especially notable increases have been reported during the current year.

A detailed survey shows that the region of highest morbidity within the reich changes from one year to the next in a desultory manner. An explanation of the erratic fluctuations in the waves of anterior poliomyelitis is to be found in the immunity against repetition of infection conferred by recovery. Thus only after a new generation of children has arisen will the contagion again encounter a large number of susceptible persons. However, the morbidity of poliomyelitis even in times of epidemic never suffices to immunize the entire population, since the disease is, after all, rare. This is shown by the following comparison: In 1937 there were 2,723 cases of poliomyelitis against 146,733 cases of diphtheria. Accordingly it must be that the majority of children either are not susceptible to infection by the agent of poliomyelitis or do not react to this infection in such a way as to produce the typical disorder with its concomitant paralysis. Even the so-called silent infections can confer immunity against later contagion. "Silent" infections are much more frequent than the forms that run a severer course.

With the end of the short-lived seasonal wave the local prevalence of the contagion tends to subside and soon disappears almost completely. The location and severity of the next year's epidemic cannot be foretold. A strong impetus has recently been given to investigation of the many as yet unsolved problems relative to ways and means of combating poliomyelitis. A new plan of therapy, based on uniform points of view, has been instituted in the hospitals of Berlin and of Hamburg. The experimental studies are concerned with the determination of the protective value of convalescent serum. Attempts have also been made to determine for how long and in what quantity protective substances are present in human beings following recovery from poliomyelitis as well as the protective value of the serum of healthy persons from the environment of patients with poliomyelitis. Finally, closer studies of the virus have been attempted by its cultivation. Only within the next few years will the results of this research be evaluated.

#### The Number of New Medicaments in Germany

The association of manufacturers of chemical-pharmaceutic preparations, an organization that represents thirty-seven leading German firms, reports that during 1935, 1936 and 1937 a total of 174 new specialties were placed on sale, whereas 108 specialties were withdrawn from the market. Accordingly the total number of these firms' pharmaceutic products on the market during the past three years increased by sixty-six. On April 1 these firms had 1,314 specialties on the market; if particular medicinal forms are considered, this total reaches 1,969.

Judging by the flood of pharmaceutic products in the German market, the quoted figures suggest that pharmaceutic houses both inside and outside the manufacturers' association bring out a vast number of so-called pharmaceutic agents (*arzneimittel*), which for the most part contain no new principle but rather—and this is still considered good form—merely represent the same or similar products under new names. In any event the regulation of the pharmaceutic industry, long urged by representatives of the medical profession, has not yet taken place, even with regard to the public declaration of every pharmaceutic product prescribed by a physician.

#### The Importance of Ewe's Milk in the Diet

Ewe's milk in the diet was the object of investigations undertaken by the Breslau University institute of animal husbandry and milk economy, the experimental research station for animal husbandry at Kraftborn and the Breslau Municipal Hospital for Nurslings and Infants. The principal investigators were

W. Zorn, F. Richter and C. Wiener. With respect to the importance of ewe's milk in the national food economy it was estimated that there is an annual world yield of 5 billion liters, as against 17 billion liters of goat's milk and 270 billion liters of cow's milk. Europe produces 44 per cent of all ewe's milk and thus stands far ahead of Asia and Africa. Of all European countries Italy is the largest producer of ewe's milk, the yield there being 620 million liters yearly; Germany produces only 20 million liters of ewe's milk yearly (as against 24 billion liters of cow's milk).

To determine the suitability of ewe's milk as a food for nurslings, the investigators carried on feeding experiments, the results of which are reported in the journal *Ernährung*. The quality of ewe's milk with respect to its ingredients is greatly dependent on the state of lactation, even in comparison with cow's milk and human milk. Ewe's milk is far superior to human milk and cow's milk in fat, protein and mineral content and consequently in caloric content. Further questions studied were whether nurslings previously nursed by the mother ought to be put on ewe's milk, whether children who have been receiving cow's milk should be given ewe's milk instead and whether dyspepsia in nurslings can be dietetically treated with ewe's milk. It was found that artificial feeding of nurslings with ewe's milk is readily practicable and that it is even more easily accomplished and leads to better results than feeding with cow's milk. Even if the nurslings were suddenly taken off cow's milk and placed on ewe's milk, the substitution was always satisfactorily accomplished, and if the babies had been affected with acute gastro-enteric catarrh when fed with cow's milk quick remission of this dyspepsia took place when they were fed with ewe's milk.

#### Appointment to Chair of Psychiatry at Berlin

A short time ago Prof. Karl Bonhoeffer, since 1912 ordinarius in psychiatry at Berlin and now 70 years old, was retired from his post. Bonhoeffer had an excellent record as director of the clinic for psychiatric and nervous diseases at Berlin University. He performed pioneer work in the fight against alcoholism, and his views on the treatment of alkaloid addictions was fundamentally accurate. He also originated the doctrine of "exogenic reaction types."

Prof. Max de Crinis, erstwhile ordinarius in psychiatry at Cologne, has been appointed to succeed Professor Bonhoeffer. De Crinis is 49 years old. An Austrian by birth, he served formerly as extraordinary professor at the University of Graz, Austria. In 1934, after his Nazi sympathies had cost him his post in Graz, he was called to Cologne. He has worked on epilepsy and the histopathology of intoxications as well as on other histologic problems concerning nerve tissue.

#### Prof. Franz Volhard Has Retired

The professor of internal medicine at the University of Frankfort on the Main has been retired, having reached the age limit of active service, 68 years. A pupil of Riegel at Giessen, Volhard first served as senior physician in large hospitals at Dortmund and at Mannheim. In 1918 he became ordinarius in internal medicine at Halle on the Saale and in 1927 he assumed a similar post at Frankfort on the Main. His greatest contributions to internal medicine were above all in the field of gastric, circulatory and kidney disorders. In 1899 he discovered the lipolytic ferment of the stomach. He engaged in a vast amount of research on hypertonia, especially the interrelation of hypertonia and diseases of the circulation and the kidneys. Volhard has become best known for his work in the field of kidney diseases. One need only recall the Volhard specific gravity test of renal function. Volhard's treatise on Bright's disease, written in collaboration with Fahr, has enjoyed wide dissemination and recognition. The testing of renal function has been vastly improved and promoted by Volhard.

## AUSTRALIA

(From Our Regular Correspondent)

Nov. 12, 1938.

## The People and Socialized Medicine

After a hard fight and bitter contest, the labor government in New Zealand, despite the well organized campaign and extensive publicity of the nationalist opposition, has won a sweeping victory at the polls. At the last elections in 1935, labor came into office with a large majority, not because of its own policy but because it reaped the benefit of a popular reaction against the nationalist government. The main issue of the elections was the character and extent of social—or socialist—legislation. Mr. Savage took his stand on the social security act (in which provision is made for universal free medical service, increased pension allowances and unemployment insurance) and extended government control of banking policy. The opposition championed private enterprise against labor socialism, attacking the proposed extension of social services as financially unsound and advocating a more modest scheme of social benefits. In this it had the active support of the British Medical Association in New Zealand, which association indeed played a most active part in the election campaign. The people, however, have recorded a heavy vote in favor of state control. The official reaction of the medical profession to this position is uncertain. Before the elections the association in New Zealand had broken off all discussion with the government on health insurance matters, after the government's rejection of the association's proposals.

## Law Relating to Abortion

The artificial interruption of pregnancy by a medical practitioner in a recent case of incest in South Australia has occasioned much discussion in medical and other circles as to the legal grounds for the termination of pregnancy after rape or incest. The law in this country is as follows: "Any person who, with intent to procure the miscarriage of any woman, whether she be or be not with child, unlawfully administers to her, or causes to be taken by her, any poison or other noxious thing, or unlawfully uses any instrument or other means whatsoever with the like intent shall be guilty of felony, and liable to imprisonment for life." The use of the word "unlawfully" implies that Parliament had in mind that such an act might be done "lawfully" if it was necessary to preserve the life of the mother, which in practice means her health and sanity, for, without either, life is worthless. The judge in the Bourne case in England, addressing the jury, said that it was obvious that the act if done by skilled persons without risk to the patient and on purpose to save the life of the mother must be lawful. The law did not permit the termination of pregnancy except for the purpose of preserving the life of the mother, but those words ought to be construed in a reasonable sense. If the physician was of the opinion, based on reasonable grounds and on adequate knowledge, that the continuance of pregnancy would probably make the woman a physical or mental wreck, the act was lawful. The law, however, does not permit the termination of pregnancy for humanitarian or eugenic reasons.

In the recent case of incest, the medical practitioner concerned brought the circumstances to the notice of the council of the South Australian Branch of the British Medical Association. After giving evidence in the police court that the girl was twenty-six weeks pregnant, he, who had been subpoenaed, requested the magistrate to receive from him a recommendation to be forwarded to the branch council. In this it was recommended that, in consideration of the very grave doubt as to the future mentality of the child to be born and the danger to the future health and mental state of the child mother, physicians learned in such matters should confer with a view to ensuring nonsurvival of the infant. The council, however, has emphatically asserted in a public statement that it is not its province officially to advise members of the branch on the professional

care of individual patients. It was pointed out to the practitioner concerned how the opinion of specialists might be obtained to determine whether the birth of the girl's child was fraught with danger to the life of the mother. No further action by the council was deemed necessary. Although it is realized by the council that public opinion is immensely and medical opinion is much in favor of the legal termination of pregnancy in cases of rape and incest, it has not yet considered what action, if any, should be taken in respect to alteration of the law concerning abortion.

## Marriages

JOHN RICHARD HEATON, Hoopeston, Ill., to Miss Edyth Eleanor Clawson of La Fayette, Ind., October 29.

ROBERT A. HARE, Baltimore, to Miss Anne Lee Mead of Berkeley, Calif., in Alexandria, Va., October 23.

EUGENE LLOYD WENK, Cloutierville, La., to Miss Cammie Henry of Melrose in Alexandria, September 23.

ALFRED DEADERICK DOAK, Shelbyville, Ky., to Miss Evelyn Marie Cowan of Fayetteville, Tenn., in October.

LEWIS WILLIAM HAGNA, Marion, N. C., to Mrs. Evelyn Mentzer Innes of Huntington, Pa., in October.

JAMES GILBERT MASON WEYAND, Rochester, Pa., to Miss Susan Gallup of Beaver Falls, October 22.

RICHARD E. HOUSNER, Richland Center, Wis., to Miss Ardyce Kotvis of Hillsboro, October 30.

ROBERT WILLIAM BARRETT, Lexington, Mass., to Miss Alice Frances McNamara of Allston recently.

HERBERT PAUL DEXHEIMER, O'Fallon, Ill., to Miss Doris McGilligan at Tower Hill, October 29.

WILLIAM FREDRIC DELP to Miss Dorothy Elizabeth Wallner, both of Pulaski, Va., November 15.

DANTE PETER DAPOLONIA, New York, to Miss Buena Jones of West Point, Ga., September 30.

SAMUEL A. FREITAG to Miss Alice Elizabeth Kimball, both of Janesville, Wis., November 4.

ARTHUR ROWELL DAHLGREN, Atlanta, to Miss Jane Hartzog of Los Angeles, October 30.

WILLIAM R. BAKER to Miss Mary Corine Jaillet, both of Atlanta, Ga., in September.

OWEN C. CLARK, Oconomowoc, Wis., to Miss Grace Gasper of Waukesha, November 5.

LESTER J. BUIS, Pender, Neb., to Miss Isabel Connolly of Muncie, Ind., August 14.

GLENN S. EDGERTON, Hickory, N. C., to Miss Sylvia Steele of Statesville in October.

RALPH V. EVERLY, Indianapolis, to Miss Ruth L. Black of Brownstown, October 28.

LAWRENCE H. DONATH to Miss Mary Masters, both of Lake Geneva, Wis., October 1.

HENRY SARGENT HOWARD to Miss Louise Flora, both of Peoria, Ill., October 20.

GILBERT W. BENJAMIN, Baltimore, to Miss Doris Sundmacher at Radnor, Pa., recently.

CHARLES E. WALL to Miss Dorothy Burns, both of Manitowoc, Wis., October 8.

CLARK E. BAKER, Marion, Ill., to Miss Mary Rodd of St. Louis, September 10.

RAYMOND R. REMBOLT to Miss Mac Street, both of Lincoln, Neb., September 11.

GEORGE H. WEGMANN JR. to Miss Betty Sacia, both of Milwaukee, October 15.

RALPH VINJE to Miss Evangeline Kelley, both of Bismarck, N. D., October 27.

RALPH COHEN to Miss Paula Doris Josephie, both of New York, October 14.

TALCOTT BATES to Miss Margaret S. Pardee, both of New York, October 13.

SAMUEL BISHOP HUGHES, Wildwood, N. J., to Miss Anne Weber recently.

JOHN SEARLE GIFFIN to Miss Betty Burk, both of Waterloo, Iowa, October 8.

SIDNEY BERMAN to Miss Beatrice E. Kay, both of Detroit, October 22.

## Deaths

**James Allen Jackson** ☉ Danville, Pa.; Jefferson Medical College of Philadelphia, 1906; Member of the House of Delegates of the American Medical Association, 1932-1937; fellow of the American College of Physicians; member of the American Psychiatric Association; teacher of neurology and psychiatry, Temple University School of Medicine, 1918-1920; superintendent of the Danville State Hospital; formerly associate editor of the *Atlantic Medical Journal*; editor of the *Mental Health Bulletin* published by the state hospital; in 1929 received the honorary degree of doctor of science from Bucknell University; aged 54; died, December 1, in the Jefferson Hospital, Philadelphia, of leukemia.

**Sterling Newton Pierce** ☉ Los Angeles; College of Physicians and Surgeons, Los Angeles, 1917; assistant clinical professor of obstetrics and gynecology, University of Southern California School of Medicine; member of the Pacific Coast Society of Obstetrics and Gynecology; fellow of the American College of Surgeons; on the staffs of the Cedars of Lebanon, Los Angeles General, California, Hollywood Clara Barton Memorial and the White Memorial hospitals; aged 51; died, September 30, of injuries received in an automobile accident.

**Chauncey Vandever Umsted**, Worcester, N. Y.; University of Pennsylvania Department of Medicine, Philadelphia, 1908; during the World War served as a member of an examining board; for many years deputy health commissioner in Yonkers; at one time visiting physician to St. Joseph's Hospital, Yonkers; aged 53; died, September 14, of heart disease and nephritis.

**William Henry Chase**, Montreal, Que., Canada; Dalhousie University Faculty of Medicine, Halifax, N. S., 1922; member of the American Association of Pathologists and Bacteriologists and the American Association of Neuropathologists; lecturer and Douglas Fellow in pathology at McGill University Faculty of Medicine and curator of the museum; aged 43; died, October 20.

**Russell Ebenezer Atchison**, Northville, Mich.; University of Michigan Homeopathic Medical School, Ann Arbor, 1900; member of the Michigan State Medical Society; for many years superintendent of the University of Michigan Homeopathic Hospital, Ann Arbor; aged 68; died, October 18, in the University of Michigan Hospital, Ann Arbor, of Parkinson's syndrome.

**Glenn Levi Whiting** ☉ Canisteo, N. Y.; University of Buffalo School of Medicine, 1904; past president of the Steuben County Medical Society; served during the World War; county coroner; member of the board of education; aged 62; on the staff of the Bethesda Hospital, Hornell, where he died, September 8, of bacillary dysentery and pernicious anemia.

**Andrew Macphail**, Montreal, Que., Canada; McGill University Faculty of Medicine, Montreal, 1891; formerly professor of the history of medicine at his alma mater and professor of pathology at the University of Bishop College Faculty; served during the World War; formerly editor of the *Canadian Medical Association Journal*; aged 73; died, September 23.

**Stephen Thomas Quinn** ☉ Elizabeth, N. J.; University of the City of New York Medical Department, 1897; fellow of the American College of Surgeons; on the staffs of St. Elizabeth's Hospital and Elizabeth General Hospital; served during the World War; aged 71; died, September 18, in the Sisters Hospital, Waterville, Maine, of bronchopneumonia.

**Edgar Nathan Cowan**, Merchantville, N. J.; Medico-Chirurgical College of Philadelphia, 1916; formerly assistant professor of biochemistry at the Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania, Philadelphia; served during the World War; aged 58; died, October 24, of chronic nephritis and uremia.

**Nathaniel Ross** ☉ Wilkes-Barre, Pa.; Jefferson Medical College of Philadelphia, 1892; past president of the Luzerne County Medical Society; served during the World War; for many years physician to the school district; on the staff of the Nesbitt Memorial Hospital, Kingston; aged 71; died, September 24.

**George McAlpin Liddell**, Waco, Texas; Baylor University College of Medicine, Dallas, 1909; member of the State Medical Association of Texas; served during the World War; city health officer; on the staff of the Providence Hospital; aged 54; died, October 23, of injuries received in an automobile accident.

**Frank Suggs**, San Antonio, Texas; Arkansas Industrial University Medical Department, Little Rock, 1897; at one time member of the medical reserve corps of the U. S. Army;

veteran of the Spanish-American and World wars; aged 63; died, September 10, of coronary occlusion and arteriosclerosis.

**Edwin Aid Layton**, Seattle; College of Physicians and Surgeons, School of Medicine of the University of Illinois, 1909; formerly medical missionary; for many years director of health of the public schools in Tacoma; aged 65; died, October 6, in the Emanuel Hospital, Portland, Ore., of myocarditis.

**Charles W. Famous**, Street, Md.; University of Maryland School of Medicine, Baltimore, 1901; member of the Medical and Chirurgical Faculty of Maryland; formerly member of the state legislature; aged 63; died, October 17, in the Union Memorial Hospital, Baltimore, of coronary thrombosis.

**Emory Hamlin Wood**, Salisbury Center, N. Y.; Hahnemann Medical College and Hospital, Chicago, 1881; member of the Medical Society of the State of New York; member of the board of education; for many years health officer; aged 78; died, September 18, of cerebral hemorrhage.

**John William Funck** ☉ Baltimore; University of Maryland School of Medicine, Baltimore, 1888; aged 84; for many years on the staffs of the Presbyterian, Eye, Ear and Throat Charity Hospital and the Franklin Square Hospital, where he died, October 4, of chronic myocarditis.

**Orlando W. Brownback**, Pendleton, Ind.; University of Pennsylvania Department of Medicine, Philadelphia, 1867; member of the Indiana State Medical Association; formerly health officer and member of the school board; aged 92; died, October 13, of chronic myocarditis.

**Marcus White Fredrick**, Brentwood, Calif.; Universität Leipzig Medizinische Fakultät, Saxony, Germany, 1888; member of the California Medical Association; formerly on the staff of the French Hospital, San Francisco; aged 77; died in September of chronic nephritis and uremia.

**Vestal Raul Abraham** ☉ Long Beach, Calif.; Rush Medical College, Chicago, 1913; fellow of the American College of Surgeons; served during the World War; on the staffs of the Long Beach Community, Seaside and St. Mary's Long Beach hospitals; aged 53; died in October.

**Arthur Horace Gordon** ☉ Chicago; Hahnemann Medical College and Hospital, Chicago, 1887; at one time professor of internal medicine at his alma mater; on the staffs of the Edgewater and Illinois Masonic hospitals; aged 75; died, December 2, of coronary thrombosis.

**Jacob Clarence Kanigsberg** ☉ Freeport, N. Y.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1926; on the staff of the Meadowbrook Hospital, Hempstead; aged 38; died, September 20, of cerebral embolism and aortic and mitral regurgitation.

**Edward Albert Packard**, Newton, Mass.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1886; member of the Massachusetts Medical Society; aged 80; died, September 8, in South Harpswell, Maine, of angina pectoris.

**Frederick Henry Wetmore**, Hampton, N. B., Canada; McGill University Faculty of Medicine, Montreal, Que., 1888; at various times had been health officer of Kings County, medical inspector of schools and coroner of Kings County; aged 76; died, September 30.

**Olin Weston Daley**, White River Junction, Vt.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1884; member of the Vermont State Medical Society; formerly member of the state legislature; aged 75; died, October 16.

**Wendell Ambrose Jones**, Riverside, Calif.; Ohio Medical University, Columbus, 1898; member of the California Medical Association; city and county health officer; served during the World War; aged 64; died, September 20, of cerebral hemorrhage.

**John Lawrence Loftus**, Old Forge, Pa.; Medico-Chirurgical College of Philadelphia, 1912; served during the World War; for many years member of the school board; on the staff of the Taylor Hospital, Scranton; aged 51; died, September 29.

**Albert Hadley Cantril** ☉ Portland, Ore.; Northwestern University Medical School, Chicago, 1902; fellow of the American College of Surgeons; aged 58; on the staff of the Emanuel Hospital, where he died, October 12, of cerebral hemorrhage.

**Benjamin Franklin Lyon**, Lancaster, Texas; University of Tennessee Medical Department, Nashville, Tenn., 1892; formerly bank president; aged 73; died, October 17, in the Dallas Medical and Surgical Clinic Hospital, Dallas, of bronchopneumonia.

**James Houston Lamb** ☉ Paragould, Ark.; Hospital College of Medicine, Louisville, Ky., 1905; past president of the Greene County Medical Society; member of the school board; aged 59; died, September 21, of carcinoma of the liver.

**Edward Perry Clark**, Los Angeles; Hahnemann Medical College and Hospital of Philadelphia, 1897; member of the California Medical Association; served during the World War; aged 64; died, September 5, of coronary disease.

**Robert Blackburn Love**, Livingston, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1900; member of the State Medical Association of Texas; aged 63; died in October of ruptured peptic ulcer.

**Charles Pender Edwards**, Asheville, N. C.; Tennessee Medical College, Knoxville, 1900; served during the World War; aged 63; died, October 6, in the Morton F. Plant Hospital, Clearwater, Fla., of cerebral hemorrhage.

**Richard S. Bradley**, Dalton, Ga.; Southern Medical College, Atlanta, 1884; member of the Medical Association of Georgia; aged 80; died, October 19, of acute dilatation of the heart and fractured neck of the femur due to a fall.

**Chester C. Copelan** \* Springfield, Ill.; Chicago College of Medicine and Surgery, 1915; served during the World War; aged 47; on the staff of St. John's Hospital, where he died, October 9, of splenic myelogenous leukemia.

**Fisher F. Demuth**, Cecil, Ohio; Eclectic Medical Institute, Cincinnati, 1882; formerly member of the state legislature; past president of the Paulding County Medical Society; aged 82; died, October 16, of cerebral thrombosis.

**Conrad William Marxer** \* Indianapolis; Central College of Physicians and Surgeons, Indianapolis, 1897; served during the World War; aged 66; died, October 15, in the Methodist Hospital of carcinoma of the sigmoid.

**Herman John Wickman**, Riverside, Calif.; State University of Iowa College of Medicine, Iowa City, 1906; member of the California Medical Association; aged 60; died, September 29, in the Riverside Community Hospital.

**Charles G. Quammen**, Mantorville, Minn.; Keokuk Medical College, College of Physicians and Surgeons, 1903; aged 64; died, September 11, at Rochester of typhoid and perforation of an ulcer of the ileum with peritonitis.

**Edward W. Wahl**, Los Angeles; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1890; served during the World War; aged 71; died, September 3, in a local hospital.

**William Wallace Winans**, Rochester, N. Y.; Hahnemann Medical College and Hospital, Philadelphia, 1899; aged 64; on the staff of the Highland Hospital, where he died, September 24, of coronary thrombosis.

**Howard Andrew Lingenfelter**, Durango, Colo.; University and Bellevue Hospital Medical College, New York, 1899; member of the Colorado State Medical Society; aged 66; died, October 23, of heart disease.

**Earl Reuben Lee**, Denver; Temple University School of Medicine, Philadelphia, 1932; member of the Colorado State Medical Society; aged 33; died, October 9, in the Fitzsimons Hospital of adenocarcinoma.

**Claud E. Chandler**, Mukilteo, Wash.; Willamette University Medical Department, Salem, Ore., 1908; member of the Washington State Medical Association; aged 55; died, October 12, in a hospital at Everett.

**Louis Herbert Maxson**, Seattle; University of Pennsylvania School of Medicine, Philadelphia, 1910; member of the American Society of Anesthetists; aged 55; died, October 3, in the Providence Hospital.

**Alfred B. Wright**, Buffalo; University of Buffalo School of Medicine, 1901; member of the Medical Society of the State of New York; aged 60; died, September 24, of cerebral hemorrhage and hypertension.

**Edward Marcelis Clark**, Mamaroneck, N. Y.; Bellevue Hospital Medical College, New York, 1885; member of the Medical Society of the State of New York; health officer; aged 76; died, September 10.

**Walter P. Hailey**, Haileyville, Okla.; Missouri Medical College, St. Louis, 1899; aged 62; died, September 12, in the Albert Pike Hospital, McAlester, of calcification of the pineal gland and angina pectoris.

**Frederick Victor Lyman**, Velva, N. D.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1903; aged 59; died, October 29, in a hospital at Minot of cerebral hemorrhage.

**William Elmer Boyer**, Newark, Ohio; Starling Medical College, Columbus, 1897; member of the Ohio State Medical Association; aged 68; died, October 4, of nephritis and Parkinson's disease.

**Graham Lawrence**, Shelbyville, Ky.; University of Louisville Medical Department, 1892; member of the Kentucky State Medical Association; aged 68; died, October 7, of cardiac thrombosis.

**Alois J. Blickhan**, Quincy, Ill.; Keokuk (Iowa) Medical College, 1891; member of the Illinois State Medical Society; aged 74; died, October 20, of arteriosclerosis and hypostatic pneumonia.

**Frederick Richmond McBrien**, Niagara Falls, N. Y.; Trinity Medical College, Toronto, Ont., Canada, 1891; aged 69; died, September 23, of uremia, pulmonary edema and nephritis.

**Edward Hardaway Manson Parham**, Lordsburg, N. M.; Medical Department of Tulane University of Louisiana, New Orleans, 1898; aged 61; died, September 10, of organic heart disease.

**Frank Heywood Stocker**, West Hartford, Conn.; New York Homeopathic Medical College and Hospital, 1897; aged 62; died, October 9, at the Hartford Hospital of lobar pneumonia.

**James Roy Bierly** \* Peoria, Ill.; Chicago College of Medicine and Surgery, 1911; served during the World War; aged 55; on the staff of the Proctor Hospital, where he died, October 18.

**E. C. McComas**, Flat Top, W. Va.; Tennessee Medical College, Knoxville, 1901; Maryland Medical College, Baltimore, 1904; aged 63; died, October 18, of acute dilatation of the heart.

**Lealon Edward Lamb** \* Clinton, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1928; aged 37; died, October 7, in the Menorah Hospital, Kansas City, Mo.

**John Charles Stewart**, Philadelphia; Hahnemann Medical College of Philadelphia, 1903; aged 54; died, September 16, of asphyxiation due to pressure from a deformity of the spine.

**James Joseph P. Armstrong** \* Douglas, Ariz.; Trinity Medical College, Toronto, Ont., Canada, 1893; aged 67; died, September 30, in La Jolla, Calif., of cerebral hemorrhage.

**Alson David Ferris**, Hardwick, Vt.; University of Vermont College of Medicine, Burlington, 1905; aged 71; on the staff of the Hardwick Hospital, where he died, October 5.

**George R. Clayton Jr.** \* La Fayette, Ind.; Illinois Medical College, Chicago, 1909; served during the World War; aged 54; died, October 17, of acute coronary thrombosis.

**Elliott Vanveltner Converse**, Palestine, Texas; Rush Medical College, Chicago, 1902; on the staff of the Missouri Pacific Lines Hospital; aged 59; died, October 8.

**Henry Walter Lilly**, Fayetteville, N. C.; Bellevue Hospital Medical College, New York, 1879; for many years bank president; aged 82; died, October 11, of myocarditis.

**Wilson R. Cushing**, Dublin, Va.; University of Maryland School of Medicine, Baltimore, 1881; member of the Medical Society of Virginia; aged 81; died, October 6.

**Seth Marion Angle**, Jackson, Mich.; Detroit College of Medicine, 1906; aged 64; died, October 4, in the W. A. Foote Memorial Hospital of intestinal obstruction.

**Oshea Stowell Brigham** \* Toledo, Ohio; Long Island College Hospital, Brooklyn, 1876; aged 86; died, October 16, of chronic myocarditis and acute bronchitis.

**Otto Kothe** \* Callicoon, N. Y.; University and Bellevue Hospital Medical College, New York, 1899; served during the World War; aged 61; died, September 27.

**William B. Marks**, Augusta, Ga.; University of Georgia Medical Department, Augusta, 1883; aged 76; died, October 11, of hypertension and coronary occlusion.

**William H. Barkley**, Cold Spring, Ind.; Cincinnati College of Medicine and Surgery, 1887; aged 82; died, October 24, of mitral stenosis and chronic prostatitis.

**John B. Mahan**, Cincinnati; University of Louisville (Ky.) Medical Department, 1889; aged 78; died in October of arteriosclerosis and cerebral hemorrhage.

**Thomas Edmund Fitzgerald**, Brooklyn; Cornell University Medical College, New York, 1904; died, September 10, in Cortland, N. Y.

**Thomas D. Tharpe**, Portsmouth, Va. (licensed in Virginia in 1908); aged 72; died, September 29, of coronary thrombosis.

**Ernest McNeill**, New York; Bellevue Hospital Medical College, New York, 1895; aged 66; died, September 6.

**J. E. Sutton**, Viola, Ark. (licensed in Arkansas in 1903); aged 69; died, September 21, of myocarditis.

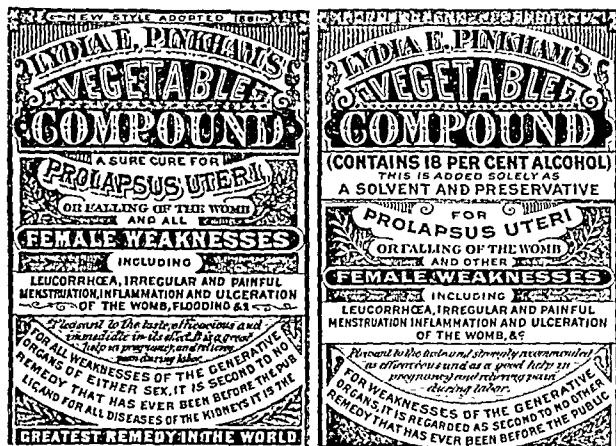
**Willis A. Clark**, Cumby, Texas (licensed in Texas, under the Act of 1907); died, September 13.

## Bureau of Investigation

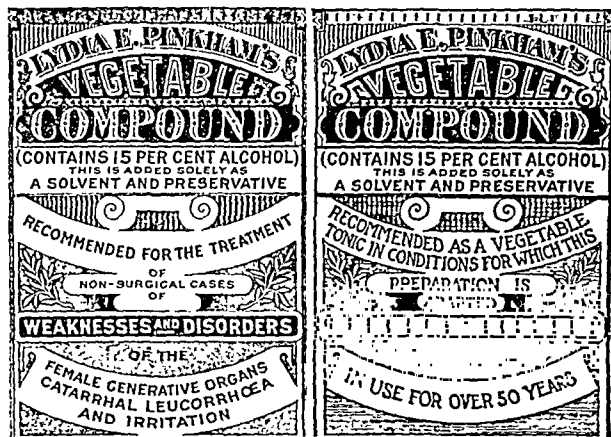
### LYDIA E. PINKHAM'S VEGETABLE COMPOUND GETS ANOTHER NEW DRESS

The carton labels of "Lydia E. Pinkham's Vegetable Compound" have been modified many times as a result of the activities of the Food and Drugs Act of 1906 as amended, and subsequent citations in connection with its enforcement. The cuts (below) showing the labels which have appeared since 1900 are not new to the readers of THE JOURNAL. In an article by Dr. Arthur J. Cramp in *Hygeia* for November 1935 concerning this preparation, it was stated:

"It will be noted in the oldest label reproduced at the time that fraudulent statements on the trade package were merely immoral instead of illegal and potentially expensive—that Lydia Pinkham's Vegetable Compound was claiming to be 'A Sure Cure for Prolapsus Uteri or



Falling of the Womb, and All Female Weaknesses,' listing a number of interesting, if intimate, conditions. Following the passage of the law, the line on the label reading 'A Sure Cure for' was deleted, and the information that the law required, giving the amount of alcohol present (at that time 18 per cent), was declared. The label still implied, however, that the Pinkham preparation was a cure for falling of the womb and many other serious conditions. It was on the basis of these claims that the Food and Drug officials proceeded against the Pinkham concern, and this action brought the verdict . . . [guilty of false and fraudulent labeling].



"Following this there was another change in the label, in which the stuff was 'Recommended for the Treatment of Non-Surgical Cases of Weaknesses and Disorders of the Female Generative Organs, Catarrhal Leucorrhoea and Irritation.' About this time, also, the alcohol content was changed from 18 to 15 per cent. A little later the statement relative to 'Catarrhal Leucorrhoea and Irritation' was deleted and yet another new label was issued. Then finally came the label that is being used today, in which it is stated that Lydia E. Pinkham's Vegetable Compound is 'Recommended as a Vegetable Tonic in Conditions for Which This Preparation is Adapted.' This statement is about as informative as it would be to say that 'For Those Who Like This Sort of Thing, This Is the Sort of Thing That Those People Like.'"

Now, according to an advertisement in the *American Druggist* for November 1938, the preparation has another new label. While it is still "Recommended as a Vegetable Tonic in Conditions for Which This Preparation is Adapted," if any, it is now called "Lydia E. Pinkham's Vegetable Compound (With Vitamin B<sub>1</sub>)"—200 International Units to the Daily Dose. Just why this particular vitamin was selected by these old-timers in the "patent medicine" business is difficult to know.

Lydia E. Pinkham, of course, never heard of vitamin B<sub>1</sub>. According to the Council on Pharmacy and Chemistry, vitamin B<sub>1</sub> is useful in correcting and preventing beriberi and anorexia of dietary origin in certain cases, and of value in securing optimal growth of infants and children, and is conceded to be a dietary essential which is of value in some conditions where difficulty in utilizing ordinary foods in the usual way is encountered. Since beriberi is only infrequently seen in the United States, and since the Pinkham preparation is obviously not for infants and children, it may be concluded that vitamin B<sub>1</sub> is added for correcting and preventing anorexia or to improve the utilization of ordinary foods where that utilization is not taking place. In view of many of the claims which have been used for the Pinkham preparation in the past, it is indeed surprising that the manufacturers, after deciding to add a vitamin, did not select vitamin E, since the latter vitamin, although not established, has been endowed with certain effects which were claimed for Lydia E. Pinkham's Vegetable Compound. How-



ever, there is no reason why the selection of the vitamin to be added to a nostrum of this type should be made on a rational basis.

The addition of vitamin B<sub>1</sub> to this old remedy is reminiscent of the change that was made in another nostrum many years ago. Quoting from THE JOURNAL for Sept. 28, 1912, it is stated in reference to "Peruna" that:

"In 1906 the Peruna company was notified that it either must put some medicine in its 'booze' or it could be sold only in saloons or other places carrying liquor licenses. The company thus found itself between the devil and the deep blue sea. If it left its nostrum as it was, it could only be sold by one who held a retail liquor dealer's license; this, of course, would at once make its real character evident to the purchaser. If, on the other hand, appreciable quantities of drugs were put into the stuff, it would spoil its sale as a beverage. Evidently believing that the preparation was so popular that nothing could hurt its sale materially, the company chose the latter course. A laxative was added and Peruna was still permitted to be sold as a medicine."

Peruna at that time contained about 20 per cent of alcohol. In 1920, however, this was reduced to 12 per cent, but in 1927 it was increased to 18 per cent and the senna was removed.

Changing formulas of "patent medicines" sold under the same name not infrequently causes considerable trouble to the user. Heavy users of Peruna probably did not appreciate its senna content. It must be granted, however, that there is probably nothing harmful in the addition of vitamin B<sub>1</sub> to Lydia Pinkham's Vegetable Compound. That there is any need for vitamin B<sub>1</sub> beyond that obtained in the normal diet, in any significant number of patients who take this "Compound," is something that is entirely unknown. It would be interesting to see exactly what type of claim is made by the manufacturer for this additional

ingredient. One is not able to determine this from the labels, since, as pointed out, the preparation is recommended in conditions for which it is adapted.

A current advertisement (cut above) may or may not refer in part or in toto to the new ingredient. Judging by this advertisement, vitamin B<sub>1</sub> may have been added for "tonic" effects, but a tablespoonful of the preparation, which has the alcoholic content of ordinary wine, may bring about certain "stepping-up" effects without the addition of any vitamin.

Another day, another label, a new age, a new ingredient, but still essentially the same old "female weakness" nostrum. Grandma used it and her daughter tolerated it, but her granddaughter should know better.

## Correspondence

### USELESS DUPLICATION IN TUBERCULOSIS WORK

To the Editor:—There is no other country in which there is more than one national tuberculosis association to combat tuberculosis in all its aspects and working in harmony with local societies, committees and specialistic organizations. Our country alone has the questionable distinction of having a number of so-called national bodies working and meeting independently of the National Tuberculosis Association. They include the American Clinical and Climatological Association, which meets annually and publishes its own transactions; the American Sanatorium Association, which meets at the same time as the National Tuberculosis Association and publishes its transactions with the latter's annual report; the Federation of American Sanatoria, which meets annually, and the American College of Chest Physicians and the American Academy of Tuberculosis Physicians, which meet also annually but like the former, independently of the meeting of the National Tuberculosis Association. The last three associations have for their official organ the monthly journal called *Diseases of the Chest*.

Before me is a letter dated Aug. 12, 1938, signed by the outgoing president, Ezra Bridge, and the incoming president, Bruce H. Douglas, of the American Sanatorium Association. In it there is first a suggestion for enlarged activities and members are asked to express their ideas concerning disbanding or enlarging and renaming the association. The letter concludes with the statement that the problem is now one of reorganization or amalgamation with the American College of Chest Physicians and the Academy of Tuberculosis Physicians. The Federation of American Sanatoria is not mentioned. The need of such a federation alongside the American Sanatorium Association, which has done such good work, is not apparent.

Why cannot all these activities be conducted under the auspices of the National Tuberculosis Association? The latter has a division for clinical section, administrative section, a pathologic section, a social work section, and so on. Nearly all phases of the tuberculosis problem except, perhaps, that of thoracic surgery are covered. This phase of phthisical therapy is so vast that there may be justification for the existence of an American Association for Thoracic Surgery, meeting separately and having its own monthly publications. Aside from that, one would think that the National Tuberculosis Association meets all the demands for considering in its program of work a complete tuberculosis therapy and prevention. Yet complaints have arisen: First, that the National Tuberculosis Association has neglected the western section of the country and particularly the interest of private sanatoriums; that the official organ of the society, the *American Review of Tuberculosis*, is too exclusive and inadequate to meet the demand for publication of many important papers on tuberculosis; that there is no criterion to judge competent specialists, and that the general practitioner has difficulty in selecting consultants when consultation is needed.

To obviate the latter condition, a number of tuberculosis physicians in the western and some eastern parts of the country united to form the American College of Chest Physicians and the American Academy of Tuberculosis Physicians and create for their official organ a monthly journal entitled *Diseases of the Chest* and publish a directory of experienced pneumothorax physicians.

If all men treating a particular part of the body should unite under the name of an academy, would it not lead to confusion, particularly in large cities, where there is usually one good academy with sections for all specialties? How bewildering would such multiplicity of academies be to the general practitioner. In tuberculosis of the lung there are already two, and a large number of good specialists do not belong to either. Heretofore the general practitioner has seemingly had little difficulty in choosing the consultant in whom he had sufficient confidence. Yet, in view of the importance of having for the young general practitioner starting out in practice an authentic guide to consult when consultation in tuberculosis is needed, I venture to quote from the letter already mentioned as one aim of the American Sanatorium Association the following: "To encourage qualified members of the organization to apply for registration with the American Board of Internal Medicine of the American Medical Association, to further the establishment by the American Medical Association of special examination, certification and registration of specialists in tuberculosis under the auspices of the American Board of Internal Medicine." This is a splendid way to clarify and solve the problem. The only suggestion I would make here is to add that the qualified member should be an expert in pneumothorax and application of pneumolysis. This would do away with the need of the directory for pneumothorax specialists. A list of consultants officially certified at the disposal of the general practitioner would be a guaranty of the competence of the consultant. While I have not the slightest doubt that the men who are members of the American College of Chest Physicians and the American Academy of Tuberculosis Physicians are equally competent as those who would pass the special examination qualifying as specialists in tuberculosis before the Board of Internal Medicine, membership in the two organizations created as a guaranty of qualification may not seem quite as secure to the young practitioner as the official list which the American Medical Association has at the disposal of inquirers.

The marvelous success in the reduction of the morbidity and mortality of tuberculosis was obtained prior to the past three years in which criticism, discontent and dissension among the workers arose. How great the result might be from united action of all the tuberculosis workers under the leadership of the officers and the Board of Directors of the National Tuberculosis Association, particularly since aided in their efforts by a benevolent United States government, the American Medical Association, the many state and local health departments, the equally numerous city and town tuberculosis associations and committees, the tuberculosis work of life insurance companies and, last but not least, all supported by an enlightened and generous public.

How very considerable a factor the United States government has already played in the antituberculosis crusade may be evident by a brief enumeration of its hospitals and sanatoriums. According to the latest Sanatorium Directory, the Veterans Administration Facilities for the care of the tuberculous ex-soldiers has no less than twenty-seven well equipped sanatoriums and all general hospitals operated by the administration have, besides, a few beds for observation and terminal cases. The U. S. Army and the U. S. Navy each has three tuberculosis hospitals; the U. S. Public Health Service operates seventeen tuberculosis hospitals and in addition to these there are six other U. S. Public Health Service hospitals which admit cases for observation and emergency care. For our Indians, our generous government has no less than fifteen sanatoriums



and thirteen general hospitals where tuberculous Indians are also admitted. Added to these government institutions the state, municipal and private sanatoriums throughout the country, we may proudly claim to have no less than 749 sanatoriums, preventoriums and general tuberculosis hospitals with a total capacity of 92,786 beds. In paying the just tribute to the splendid activities of our government, it is with equal pride that I state that no other body of civilian tuberculosis workers has achieved more success, has done more yeoman work in dealing with tuberculosis as a disease of the masses and to a very large degree is responsible for the marvelous mortality reduction of this disease than the National Tuberculosis Association.

The association elects a president every year and has a permanent secretary and treasurer. Hon. Franklin D. Roosevelt, President of the United States, is one of the association's honorary presidents. It has a board of directors of 101 which I would like to see increased by two representative physicians of the Negro race. Tuberculosis is still the medicosocial disease of the masses, attacking rich and poor alike, and among the colored population it is unfortunately most prevalent and with a seriously large morbidity and mortality. Much has been done and much is known but there is more to do and more to know.

In conclusion, I refer once more to that important letter addressed to all members of the American Sanatorium Association, which concludes as follows: "There is no doubt amalgamation of medical organizations in the tuberculosis field is desirable and that one organization of physicians interested directly and indirectly in tuberculosis should be the aim of all concerned."

S. ADOLPHUS KNOPF, M.D., New York.

16 West Ninety-Fifth Street.

## Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

### TESTING ENDOCRINE FUNCTIONING

*To the Editor:*—I should like to know about tests similar to the basal metabolic rate which indicate the normal or abnormal functioning of the endocrine glands, that is tests which determine normal or abnormal content of the various hormones of the pituitary, ovary and so on in such conditions as acne and menstrual disorders.

SOLOMON GREENBERG, M.D., Bayonne, N. J.

**ANSWER.**—The functional state of the endocrine glands can be determined in part by the following methods:

1. The amount of gonadotropic hormone in the blood and urine at the time of ovulation gives an estimate of the gonadotropic activity of the pituitary gland.
2. For the parathyroids by the fasting level of calcium and phosphorus in the blood.
3. For the pancreas by the fasting blood sugar content of the blood and by sugar tolerance tests.
4. The estrogenic content of the blood and urine during the menstrual cycle may give some indication of ovarian function. The chemical determination of urinary pregnandiol will reflect the activity of the corpus luteum.
5. For the testes by the amount of androgenic substance in the urine. In making these tests one can use any of the current methods described in any modern textbook of endocrinology (Werner, Lowenberg).

There is no pathognomonic hormonal picture associated with acne. Acne, however, is commonest at about the age of puberty. The condition is sometimes improved by the use of pituitary-like gonadotropic hormone extracts.

In all menstrual disorders it is advisable to eliminate non-endocrine factors such as debilitating diseases, blood dyscrasias and voluntary starvation for the purpose of reduction in weight. It is also important to eliminate organic lesions such as adrenocortical adenomas and pituitary adenomas.

In the absence of a nonendocrine factor or organic lesion of the endocrine glands, it is important to determine, if possible, which of the several endocrine glands is primarily responsible for the menstrual disorder. The thyroid function should be tested by means of the basal metabolism estimation and blood cholesterol.

A primary hypogonadism is determined by body measurements (relatively long extremities) and general appearance of the patient (boyish figure, usually underweight).

(a) The administration of gonadotropic substance is more effective in retarded puberty of boys with undeveloped sex organs.

(b) The postmenstrual state is characterized by the diminution or absence of estrogen and by an excess of the follicle stimulating hormone of the pituitary. Troublesome symptoms may be relieved by the prolonged administration of moderate doses of estrogen. This constitutes replacement therapy.

(c) Amenorrhea, secondary in character, if not caused by non-endocrine conditions or organic lesions of the pituitary, thyroid, adrenals or ovaries, may be overcome occasionally with low dosage irradiation of the pituitary gland and ovaries. When the uterus is hypoplastic, as it usually is in cases of amenorrhea, the administration of estrogen in large doses given intermittently is, sometimes, advisable for its stimulative effect on the muellerian tract.

(d) Menorrhagia may be controlled sometimes in those of child-bearing age by the administration of gonadotropic substance. In women at the menopause, menorrhagia may require a diagnostic curettage and the administration of radium. Progestin may be tried. It is usually ineffective.

It should be realized that the field of endocrine treatments in menstrual disorders is still largely in the stage of clinical investigation. Most menstrual disorders are best handled through the advice of a competent gynecologist.

### PANCREATIC EXTRACT IN URETERAL STONE

*To the Editor:*—What results have there been from the use of pancreatic extract in the treatment of ureteral stones?

ROBERT S. MCCENEY, M.D., Laurel, Md.

**ANSWER.**—The efficacy of pancreatic tissue extract in the treatment of ureteral calculi remains in the experimental stage. The extract, which is the residual solution after insulin has been precipitated from pancreatic tissue, was first found to possess definite vasodilator properties. According to the opinion of most investigators (Frey: *München. med. Wchschr.* 76:1951, 1929; Gley: *Presse méd.* 27:1279 [Oct.] 1929) the active agent is a hormone which is elaborated by and stored in the pancreas, passes into the blood in an inactive form, and is excreted in an active state in the urine. The so-called Frey hormone (Frey: *Ztschr. f. Biol.* 84:321, 1926) is a substance which has been isolated from urine and has properties identical with those of pancreatic extract; in pancreatectomized animals the rate of urinary excretion of this hormone has been found to be reduced 80 per cent. Whether the hormone exerts its dilatory effect by neutralizing epinephrine or by balancing an overstimulation of the sympathetic remains a moot point. Villaret (*Presse méd.* 37:633 [May] 1929), on the other hand, considers the physiologic activity of the extract due to sufficient amounts of choline, peptone and histamine which the hormone contains.

Because of its definite vasodilatory effects, Lazarus (*Urol. & Cutan. Rev.* 40:847 [Dec.] 1936) studied the efficacy of the extract in cases of impassable ureteral calculi. He reports concerning its use in eight cases of impacted ureteral calculi and two cases of ureteral stricture with associated spasm. In all cases save one he was easily able to pass dilating catheters and bougies to the renal pelvis thirty minutes after one or two 1.5 cc. injections of the extract. While Lazarus administered the extract intramuscularly, it is noteworthy that Elliot (*J. Pharmacol. & Exper. Therap.* 43:463 [Nov.] 1931) in animal experimentation found the extract to be active only when given intravenously and without effect when administered subcutaneously or intramuscularly.

Carrol (*South. M. J.* 31:233 [March] 1938) advises a dosage of from 2 to 4 cc. given intramuscularly; he reports pain at the site of injection as a constant finding, but it lasts only a short time. Generalized reactions to the drug are minimal and those reported consist merely of faintness and vertigo. The extract has been found to be effective in the treatment of renal colic due to stone, in postcystoscopic colic, in the instrumental removal of calculi in the lower ureter, and finally in the treatments for dilation of organic ureteral stricture. Carrol states that the extract produces prompt relaxation of the ureters and has borne this out by experimental hydrophorographic tracings of the normal human ureter under influence of the drug.

## CANCER OF BREAST

*To the Editor.*—A white woman aged 38 had a mass in the left breast removed. On biopsy and microscopic examination the mass was shown to be a highly malignant tumefaction composed of a cellular diffuse growth. The cells were unequal in size and shape; the nuclei were hyperchromatic and showed a large number of mitoses. The cytoplasm of the cells was either colorless or acidophilic. These cells were arranged in masses and columns and had a palisade formation. The desmoplastic reaction was reduced to but a few strands of connective tissue. In the center of some of these cells were areas of mucoid degeneration. The diagnosis was duct carcinoma of the breast (grade 3, moderately radio-sensitive). Should the entire breast be removed if no glands are present? Should radiation therapy be instituted before mastectomy? Would endocrine therapy aid the patient? What extension of life can be expected in this type of case? What is the prognosis? The x-ray report of the chest has not been received yet. The general physical condition and nutrition of the patient are good. The ears, nose, throat, heart, lungs, abdomen and extremities are normal. The blood pressure is 120 systolic, 80 diastolic. The blood count is within normal limits. The hemoglobin is 70 per cent, the red blood cell count 4,000,000. The patient has had three pregnancies going to full term and three miscarriages at two months. The blood Wassermann reaction is negative. The urine is normal. The mass was noticed in February 1938. After traumatic injury to the left breast the patient was operated on in August. The total mass measured 6.5 by 4.5 by 4 cm., covered by adipose tissue, and on cut section the mass was rather soft, was yellowish white, and had many chalky white pinpoints.

M.D., New York.

**ANSWER.**—It is evident from the record that the patient has a carcinoma of the breast. As she was operated on in August it is likely that further extension has occurred, as the tumor was removed locally even if there were no palpable nodes in the axilla. In about half the examples of carcinoma of the breast some involvement of the nodes is present, even though they are not palpable on physical examination. There is not the slightest advantage in preoperative irradiation, because any amount of radiation which can be given without serious damage to the healthy tissues will kill only a moderate percentage of the cancer cells and during the course of such preoperative irradiation further extension of the tumor into the breast tissues and the nodes is continuously taking place. A complete radical mastectomy should therefore be done immediately. After the wound is healed postoperative irradiation can be given. This increases the number of five year cures by about 10 per cent, provided the neoplasm has not already extended to the supraclavicular or mediastinal nodes; such a case is hopeless under any form of treatment. There is no evidence that any form of irradiation will completely sterilize diffuse carcinoma in the breast or in the axillary nodes; hence radical surgery at the present time is the only effective therapy of mammary carcinoma. This can be done with a cautery knife, electric spark or scalpel. There is some evidence that in advanced cases the use of the cautery or the cutting spark is preferable to scalpel surgery. In early carcinomas the scalpel method is just as effective as the others.

Endocrine therapy is useless. Prognosis is not possible in any individual case.

## OBSCURE ATTACKS OF VERTIGO

*To the Editor.*—During the last two years I have seen six cases almost exactly alike. I have seen three of these six during the last month. Vertigo of rather sudden onset accompanied by nausea and vomiting is the only symptom. It is so severe that the patients fall down. Bed rest and sedation halt the nausea and vomiting but have little effect on the vertigo. In each case physical examination has failed to reveal any hint as to the cause. No disturbance in hearing was present and no abnormality of the external ear or ear drum could be found. The highest blood pressure in the group was 130 systolic; 80 diastolic. No obvious focal infection was demonstrable and no history of previous medication or illness was obtained. The duration of the disease varied from five to twelve days and no recurrences have been seen. I have been unable to arrive at a diagnosis other than labyrinthitis and since I am in general practice in a small town I am unable to account for the frequency of these cases. Any information on this point as well as a better diagnosis, etiology and treatment will be appreciated. Two females aged 11 and 50, and four males aged 9, 38, 40 and 60 were affected.

FORD F. KEPPEN, M.D., Three Oaks, Mich.

**ANSWER.**—Since all the patients recovered after a brief illness and there were no recurrences, the more serious organic lesions are obviously ruled out and the disturbance must be assigned to the vestibular system, including either the labyrinth or the vestibular branch of the eighth nerve. Many toxic substances and conditions, notably tobacco, alcohol, uremia and intestinal absorption, cause vertigo, partially at least through the effect on the labyrinth, so it is logical to assume that bacterial toxins can also produce a labyrinthitis. This is seen in encephalitis, in which, however, there may be neuritis as well as direct toxic action.

Israel S. Wechsler (*A Text-Book of Clinical Neurology*, ed. 2, Philadelphia, W. B. Saunders Company, 1931, p. 276)

describes Gerlier's disease, an obscure condition in which vertigo is one of the principal symptoms. It is a rare disease occurring in certain areas of Europe as well as northern Japan, appearing only in the summer months, affecting mainly robust persons, coming in attacks which are repeated for a time and ultimately disappearing without recurrences. There are, however, usually ocular symptoms and muscular impairment.

The inquirer's description would fit certain prolonged migraine states were it not that they are single attacks. It therefore can probably be classed as a Ménière syndrome resulting from toxic labyrinthitis. In such attacks vertigo may be so severe that the patient clings to the side of the bed to remain in it or occasionally reports complete revolution of the bed or room.

Examination for nystagmus would be valuable and information as to the side to which the patients fall. Rotation tests, if suitable apparatus is available, would also be helpful.

## RECURRENT STOMATITIS

*To the Editor.*—A male about 18 years of age has stomatitis caused by yeast hyphae—*Leptotrichia buccalis*. The canker sores occur in the tongue, and on the inside of the cheek and lips. They clear up for a time and then recur. He has had this condition for a long time. I have tried bismuth preparations, arsphenamine and silver nitrate without avail. Could you suggest some treatment which might be effective?

HAROLD F. HULBERT, M.D., Dansville, N. Y.

**ANSWER.**—Since the stomatitis has resisted local therapy and has repeatedly occurred after treatment, it would seem best to look for and correct an underlying condition. It is quite possible that the yeast organism is a saprophyte existing only because of a local decreased resistance.

It would be well to be sure that the Wassermann reaction is negative and that a pulmonary involvement does not exist in conjunction with the stomatitis.

Occasionally a change in the amount of gastric acidity will clear the mouth of local lesions. Test the fasting gastric contents for the degree of free acidity. If a hyperacidity or hypoauidity is present, give an appropriate alkali or acid in the usual form to counteract the abnormality.

If this simple therapy fails, obtain cultures of the dominant organisms in the stool and make a cutaneous test, using these antigens as well as one prepared from the mouth culture. Desensitization to the organisms producing positive cutaneous reactions may result in a changed susceptibility and healing of lesions in the gastrointestinal tract.

Other mouth washes than those named can be used, such as aqueous solutions of thymol (1 to 1,000) or solution of hydrogen peroxide from 1 to 4 per cent, which are sometimes effective.

## TORTICOLLIS

*To the Editor.*—A Negro aged 44 complained that he "couldn't keep his face turned in front." He said that this condition had prevailed for four months. Examination showed that his chin stayed on the deltoid muscle of his left shoulder. He can turn his head and face forward only by using his hands. On removal of his hands it will snap back to the original position. There is one point of relaxation: when he drinks water, his head will stay quiet. The Wassermann reaction is negative; there is no deviation of the tongue, and eye convergence is normal. The patient neither smokes nor partakes of alcoholic beverages. All infected teeth have been removed. He gives evidence of perfect health otherwise. He has been receiving scopolamine hydrobromide one one-hundredth grain (0.00065 Gm.) for the last month triweekly. Please suggest treatment and references on this subject.

M.D., Missouri.

**ANSWER.**—The patient has a condition resembling a tonic torticollis or tic in which not only the right sternocleidomastoid muscle is at fault but the trapezius, splenius, scaleni and deep cervical muscles participate. Nearly all such cases are functional; that is, are not due to organic disease. They occur in persons who have a neuropathic diathesis. The fact that the patient's head will stay quiet when he drinks water indicates that there is no interference with function. There should be a complete neurologic examination to rule out any organic disease of the brain, spinal cord or cervical roots. If an organic lesion is present, one may do one of the operations described for that condition. Inquiry should be made in detail into the past history of the patient as well as with regard to the onset of the difficulty, because if a cause can be discovered the treatment must be directed to its removal. If no cause can be found, the following is suggested: Exercises in front of a mirror for five to ten minutes twice daily, the patient balancing a glass of water on top of his head; faradic current to the neck muscles on the left side of the patient once daily; supporting apparatus in the form of a pasteboard collar or a brace to be worn only in the daytime. Oppenheim's *Textbook of Nervous Diseases*, volume 2, is recommended for reference (pages 1246 to 1254).

## DANGERS FROM PYRENE FIRE EXTINGUISHERS

*To the Editor:*—A pyrene fire extinguisher was used May 17 to put out a fire in a narrow hall in which the ventilation was poor. The fire was caused by a paperhanger's gasoline steamer, which was used to steam off the paper on the wall. The steamer caught fire and caused a blaze in an area measuring 3 by 4 feet. About a quart of pyrene was used. Immediately afterward my patient had difficult breathing, became cyanotic and had gastrointestinal disturbances such as flatulence and inability to digest food. These symptoms became worse about the tenth day. Cyanosis, labored respiration, flatulence, indigestion and a rapid pulse, 120, were noticed as well as a strong taste of pyrene. An area of about 4 cm. around the patient's anus was red and inflamed. Supportive treatments such as digitalis, glyceryl trinitrate and strychnine were used with liquid and soft diet. Aromatic spirit of ammonia was used for the difficult respiration, this proving the most satisfactory stimulant. Four weeks later the patient noticed that the maxillary and ethmoid cells were blocked. When these were opened and drainage established, a taste and smell of pyrene were again noticed with a recurrence of symptoms. They subsided and the patient felt better. July 12 he took some sodium phosphate for constipation and again had a recurrence of symptoms, especially the difficult breathing, which is most noticeable at night. A roentgenogram was taken of the chest. The heart is normal in size; there is some infiltration about the hili of the lungs but this has been present for years. Now the patient's pulse is normal but he still has some difficulty in breathing at night and some cyanosis. What effect would pyrene mixed with gasoline have on the organs and structures of the body? What chemistry is involved in this condition? What change if any should be instituted in the therapy? G. J. SEARLE, M.D., Mansfield, Ohio.

**ANSWER.**—It appears probable that under the influence of heat the carbon tetrachloride of the pyrene was in part decomposed into phosgene. As little as 4 parts of phosgene per million of air may be injurious. The reason for the greater toxicity of phosgene over hydrochloric acid is probably that phosgene is absorbed as such and the toxic effects are relatively slight in the upper air passages where there is little moisture. The effect reaches its maximum in the alveoli, where the moisture content is much higher and the liberated hydrochloric acid causes corrosion. This probably explains the greater toxicity of phosgene as compared with comparable amounts of hydrochloric acid. Ordinarily phosgene action is delayed for a few hours but it may appear immediately. Its chief action leads to pulmonary edema and cyanosis. Ordinarily these manifestations are associated with a sense of constriction of the chest, coughing, nausea and vomiting. Pneumonia may appear and occasionally lung abscesses. Few patients die if they survive the first three days and escape serious sequels.

In the present instance the development of the sinusitis is undoubtedly on an infectious basis. At this late time there is no treatment with reference to the specific cause. At the outset of this type of case the patient should be placed absolutely at rest and given oxygen inhalation, and external heat should be applied. The use of digitalis as was administered in this case is commendable. The irritating cough should be diminished through the use of usual types of respiratory sedatives.

In this accident there is little reason to believe that any combination took place between escaping gasoline and carbon tetrachloride. Recurring taste of pyrene is believed to be unimportant, as little if any of this substance is retained in the nasal cavities. This type of accident is prone to provoke neuroses, but in this instance they should be dispelled through the knowledge that there is reasonable assurance that complete recovery will take place and within a short period. See also *Queries and Minor Notes* in *THE JOURNAL*, July 30, 1938, page 469.

## HYPERTONIC DEXTROSE SOLUTION IN PULMONARY EDEMA

*To the Editor:*—At this hospital it is almost a routine practice to administer hypertonic dextrose (50 cc. of 50 per cent solution) intravenously in the treatment of acute pulmonary edema and of right heart failure. No one has thus far been able to give me a satisfactory physiologic explanation for its use, nor have I been particularly impressed clinically by its results either alone or in conjunction with other methods. Is there a rationale behind this treatment or am I right in asserting that it is actually deleterious in that it throws an additional burden on an already overloaded circulation? M.D., New York.

**ANSWER.**—The administration of hypertonic dextrose solution intravenously in pulmonary edema and in failure of the right side of the heart is of certain value in some cases. The hypertonic solution takes up water from the tissues and may take enough fluid from the lungs to cause a symptomatic improvement. With normal kidney function and normal volume of blood flow through the kidneys the fluid taken up is excreted promptly and there is no increase in blood volume provided it is not given too rapidly. In cases of impaired kidney function it is always possible that there may be an increase in blood volume and that the increased blood volume might force an additional load on the heart. The additional dextrose content

is supposed to be of value to the heart muscle, although under ordinary conditions it is probable that sufficient dextrose is being supplied normally.

As in the case of other therapeutic procedures which are effective, the administration of a hypertonic solution of dextrose may do harm as well as good and the indications and contraindications for its use must be carefully weighed in each individual case. When the edema is paroxysmal and due to a temporary coronary insufficiency, for example, it may be of value. In coronary occlusion with an infarcted heart muscle the increased blood volume might do harm.

## X-RAYS CONTRAINDICATED FOR CARCINOMA OF LIVER

*To the Editor:*—A man aged 52 had five successive typical stone in the common duct gallbladder attacks the first week in August 1938 preceded by two weeks of progressive jaundice. September 8 a primary adenocarcinoma of the gallbladder and its duct with metastases to the surface of the right lobe of the liver was revealed at operation; the metastatic liver area was about 3 by 4 inches. Freeing of some two adhesions from the gallbladder duct produced a flow of bile with decided decrease in itching and an increase in appetite, but it is doubtful whether it will last. Could high voltage roentgen therapy be used here with advantage, offsetting the possible liver damage? Further operative procedures are, of course, out of the question, even drainage of the gallbladder which was so far below and back that a drain would kink. Is there any specific for the itching in severe jaundice? I have tried about everything but would appreciate any suggestions. Do you know of any two or three "appetizers" for carcinoma patients? One other complaint is that everything tastes sweet, even the water. M.D., Ill.

**ANSWER.**—Roentgen therapy is of no value in the treatment of either cancer of the gallbladder or cancer of the liver. This procedure is definitely contraindicated in the treatment of cancer of the liver. There are no specific therapeutic agents for the relief of itching in severe jaundice. There are no appetizers which are specially useful for carcinoma patients.

## UNUNITED FRACTURE AND SYPHILIS

*To the Editor:*—An unmarried white man aged 28 consulted me six months ago for treatment of a recently fractured toe (metatarsal bone). The toe was slow to heal and even now the fracture line is still clearly seen transversely through the middle third of the bone. Some callus is naturally present but calcification is not complete. The delayed union led me to suspect latent syphilis. The patient admitted that in 1935 he had three rather painless lesions on the penis for which he sought medical advice. He was sent to a laboratory for smears which he believes were reported negative; nevertheless he was given nine "shots" of an intravenous preparation but no more thereafter and no other treatment. A Wassermann test made recently was negative. Because he complained of visual disturbance he was referred to an ophthalmologist, who noted an inequality in the size of the pupils, which reacted slowly to light; a choroiditis was reported. On receiving this report I made a spinal puncture and found the fluid clear and not under increased pressure. The cell count was from two to three cells with a slight trace of globulin. The Wassermann test was negative but the colloidal gold curve was 0003330000. What is your interpretation of these observations? Do you think antisyphilitic treatment is indicated? If so, would you recommend trypanamide in view of the eye examination? M.D., California.

**ANSWER.**—There is no clear relationship between ununited fracture and syphilis. The most recent detailed orthopedic studies indicate that syphilis is in relatively uncommon association with ununited fracture and that nonunion is much more often due to other causes. It is, however, undeniable that in a few instances syphilis may be concerned in the causation of non-union of fracture.

The history of penile sores in 1935 is only suggestive of the diagnosis of syphilis and is by no means certain. About 50 per cent of all penile sores are syphilitic; the other 50 per cent are not syphilitic in character. This particular patient was treated on suspicion for early syphilis without a definite dark field or serologic diagnosis, and it is by no means certain from the history given that the nine "shots" were actually treatment for syphilis or were some other type of medication.

The ophthalmologic abnormalities recently discovered are also not diagnostic of syphilis. The slight inequality of the size of the pupils and the sluggish light reaction may be found in normal persons. Choroiditis may of course occur as a result of many causes of which syphilis is only one.

The abnormal colloidal gold curve cannot be definitely interpreted in view of the fact that the spinal fluid was otherwise normal. The particular reading of the gold curve reported suggests that this may be laboratory error.

On the basis of the facts given, no conclusion can be reached as to whether the patient does or does not have syphilis. The desirability of treatment and the type of treatment, if any is to be given, could be determined only after competent syphilologic consultation.

## IDIOSYNCRASY TO ATROPINE EYE DROPS

To the Editor:—To a girl in good health I gave 2 grains (0.13 Gm.) of atropine sulfate in one-half ounce (15 cc.) of water. Directions were to drop one drop in each eye three times a day. Her eyes were crossing at times and I wanted to refract them. Two hours later she returned after using a drop in each eye. She was in a state of excitement with gripping in the abdomen, bowel movement, pain in the legs, temperature about 103 F., headache, and flushing of the skin over the entire body. This seemed like a typical poisoning. Is there any specific treatment? Would these symptoms occur if I used homatropine hydrobromide in her eyes for a refraction?

M.D., Texas.

ANSWER.—The solution of atropine sulfate used was somewhat less than 1 per cent, which is the usual strength employed to cause paralysis of the ciliary body preceding refraction. The patient used two drops, which contained about 0.001 Gm. of atropine sulfate. The condition following this instillation was typical of atropine poisoning.

Idiosyncrasy to atropine is frequent and small doses may produce distressing and alarming symptoms. The fatal dose is relatively large, so that, although poisoning from atropine is fairly frequent, deaths from atropine are quite rare. As little as 0.1 mg. ( $\frac{1}{1000}$  grain) may cause symptoms of atropine poisoning in susceptible persons. The smallest fatal dose is recorded as 130 mg. (2 grains), given by mouth.

Atropine poisoning may be treated by giving a solution of tannic acid or, lacking this, a strong infusion of tea leaves. *Pilocarpine hydrochloride* in 0.01 Gm. (one-sixth grain) doses may be tried. This is repeated if necessary until the mouth is moist. Small doses of morphine sulfate may be given cautiously for excitement; for depression, if present, caffeine may be given.

Homatropine hydrobromide in amounts that would be used for ciliary paralysis does not induce systemic poisoning nor is there the tendency to produce or aggravate a condition of glaucoma, since the paralysis is of so much briefer duration. Homatropine does not produce delirium or mental excitement.

## MENSTRUATION AND FOOD SPOILAGE

To the Editor:—It seems to be generally agreed in this locality that if women do canning, especially that part of canning concerned with the pickling of foods, while they are menstruating, the food will later spoil. I have been asked for an explanation for this phenomenon and, having never heard of it myself before, I could think of no logical reason. Is this simply an erroneous belief concerned with the old superstitions surrounding menstruation or is there actually truth in it? I would appreciate any information you might be able to furnish me either to confirm or deny this belief.

M.D., Ohio.

ANSWER.—The inquirer may be referred to the first chapter in "Menstruation and Its Disorders" by Novak or to the monumental work of Ploss "Das Weib."

As is well known, there have been and still are many superstitious and erroneous ideas concerning the menstruating woman and the menstrual flow. Among others is evidently the one that the menstruating woman or the menstrual flow will in some way spoil food. There is no scientific basis for such a belief, and so far as actual scientific study is concerned there is apparently none mentioned in the literature.

## DIABETES INSIPIDUS

To the Editor:—A girl about 18 years of age with diabetes insipidus has absolutely no complaints beyond frequency of urination, day and night, and her urgent desire for water. I have not been able to find any other trouble in either the physical or the laboratory examination. A roentgenogram of the sella turcica reveals no abnormality there. She responds to the injection of solution of posterior pituitary and also of pitressin. Before such treatment was instituted she found that she had to get up at night about twelve times, so that her rest and sleep were much disturbed. Now, while she has been under observation and taking either solution of posterior pituitary or pitressin once a day, she gets up about twice a night. Is it advisable to give the patient a hypodermic and allow her to administer pitressin to herself at home every night?

D. A. MacGREGOR, M.D., Wheeling, W. Va.

ANSWER.—A spinal puncture can sometimes be made in early cases of diabetes insipidus, primarily for diagnostic purposes but also because the occasional condition may be immediately and sometimes permanently relieved by the withdrawal of from 10 to 20 cc. of spinal fluid. The results of injection of solution of posterior pituitary are satisfactory in most cases, but such treatment has disadvantages. Disagreeable side effects are provoked, such as pallor, headache, palpitation and diarrhea. Also, the material is expensive, and if the services of a physician or nurse are required to give the frequent injections necessary the cost may be prohibitive. Patients with diabetes mellitus customarily are trained to inject themselves with insulin, and few accidents have resulted. Solution of posterior pituitary, how-

ever, like solution of epinephrine, because of local vasoconstrictor action, is less safe to place in the hands of laymen for subcutaneous use. Anaerobic bacteria, spores of tetanus and those of gas-forming organisms, if accidentally introduced beneath the skin in a region rendered ischemic by vasoconstriction, theoretically would be more dangerous, and in practice more accidental infection has occurred from injection of vasoconstricting substances than from insulin. These objections are avoided by the administration of dry, powdered substance of the posterior lobe intranasally (Smith, F. M.: Diabetes Insipidus, Treatment by Intranasal Insufflation of Posterior Lobe Pituitary Powder, THE JOURNAL [March 3] 1934, page 660), which in most cases, if repeated at sufficiently frequent intervals, is as effective as any other method of administration of pituitary.

## VASODILATORS AND HEADACHE

To the Editor:—A woman aged 56 has hypertension with evidence of coronary sclerosis. She has had persistent headaches since puberty, relieved only by hot showers directly on the head and by hot applications to the head. This headache is always aggravated by vasodilators, which have been prescribed for her from time to time. It seems that vasodilators do not exercise a selective action in this case. Since she is not a patient of mine, I do not know of any other facts. She has been treated for a long time without beneficial results. I should like to know about any similar cases and whether there is anything one might do to relieve the precordial pain without aggravating the headache and vice versa.

M.D., New York.

ANSWER.—It is not possible to be explicit with the data at hand. The effect of vasodilator drugs in causing headaches in normal persons is well known. The headache accompanying the administration of glycerol trinitrate is an example. Some cases of chronic headache might reasonably be supposed to be aggravated by such drugs. The consequent fall in blood pressure might also be a factor.

If the more rapidly acting nitrites cannot be used for the acute paroxysms of cardiac pain, the effect of spirituous liquors might be tried or strong black coffee.

For constant use between the attacks, one of the purine base diuretics might be tried, for example one of the theobromines. They produce a definite coronary vasodilator effect with minimal peripheral vasodilatation.

## IONTOPHORESIS

To the Editor:—Please give me information regarding the deposit of metals or metallic solutions in the skin by electrolysis. I am not referring to the deposit of such metals by the use of the needle but by the diffuse action of such metals. I should appreciate details of the amount of current necessary, the apparatus to be used, and so on.

M.D., California.

ANSWER.—It is doubtful whether metals can be transported across and deposited in tissues of appreciable thickness. Little more than surface deposits can be expected. There is considerable controversy on this matter in the voluminous literature, but proponents for iontophoresis have by no means presented solid, convincing evidence for the exaggerated claims which many of them make. For details of this method the inquirer is referred to the following:

Kovacs, Richard: Electrotherapy and Light Therapy, Philadelphia, Lea & Febiger, 1938.  
Hollander, A. R.: Physical Therapeutic Methods in Otolaryngology, St. Louis, C. V. Mosby Company, 1937.  
The Interrupted Low Frequency and the Constant Electric Current in Medicine, Report of the Council on Physical Therapy, THE JOURNAL, Oct. 31, 1936, p. 1469.

## LYMPHOSARCOMA

To the Editor:—I received the following report on a gland removed from the supraclavicular area. What is the prognosis and what is the best treatment for this condition? There are no metastases and the patient's general condition is excellent. This is of approximately two months' duration. Microscopic examination: The normal architecture of the lymph node is almost completely replaced by diffuse hyperplasia of atypical lymphoblasts. There are infiltrations of lymphoblasts through the capsule into the surrounding fat tissue. There are occasional eosinophils, but the absence of myeloid giant cells and fibroblasts would indicate lymphoblastoma rather than Hodgkin's disease.

M.D., Ohio.

ANSWER.—The treatment for lymphosarcoma is either by x-rays or by radium. The prognosis depends on the extent of the disease and the efficiency of the treatment. When adequate radiation therapy is administered to a localized area of lymphosarcoma there is an excellent chance of complete sterilization of the treated focus. The bad prognosis usually associated with this disease is due to the fact that there frequently exist outlying areas which are affected by the disease but which are clinically not recognizable.

## Medical Examinations and Licensure

### COMING EXAMINATIONS

#### STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, December 10, page 2235.

#### NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Medical centers having five or more candidates desiring to take the examination, Feb. 13-15, May 1-2 (Part II only—limited to a few centers), June 19-21, and Sept. 11-13. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th Street, Philadelphia.

#### SPECIAL BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: An Affiliate of the American Board of Surgery. Written examination, Part I, will be held in various cities of the United States and Canada, April 8. Oral examinations for all candidates, St. Louis, May 13-14. Applications must be filed not later than sixty days prior to the date of the examinations. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF INTERNAL MEDICINE: Written examinations will be held in various parts of the United States, Feb. 20. Application must be received on or before Jan. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: General oral, clinical and pathological examinations for all candidates, Part II examinations, (Groups A and B) will be held in St. Louis, May 15-16. Application for admission to Group A examinations must be on file in the Secretary's office by March 15. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: St. Louis, May 15. Applications must be filed before February 15. Sec., Dr. John Green, 3720 Washington Blvd., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Memphis, Tenn., Jan. 13-14. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: St. Louis, May 12-13 and Chicago, Oct. 6-7. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PATHOLOGY: Richmond, Va., April 8-9. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: New York, April 26. Appointments must be made before Dec. 26. St. Louis, May 16. Appointments must be made before Jan. 16. Cincinnati, Nov. 14-15. Appointments must be made before July 14. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 28-30. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: St. Louis, May 11-14. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: New York, Jan. 13-15. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

### California July Examination

Dr. Charles B. Pinkham, secretary, California State Board of Medical Examiners, reports the written examination held at Los Angeles, July 12-14, 1938. The examination covered nine subjects and included ninety questions. An average of 75 per cent was required to pass. One hundred and twenty-eight candidates were examined, 120 of whom passed and eight failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists.....(1935)	80.2, 81.4, 83.3, 75.6, 76.2, 78.2, 78.2, 78.2, 78.8, 79, 79.2, 79.2, 79.3, 79.6, 80, 80.6, 80.7, 80.9, 81.1, 81.3, 81.4, 82.1, 82.2, 82.8, 82.8, 83, 83, 83.1, 83.2, 83.3, 83.4, 83.6, 83.7, 83.8, 84.3, 84.3, 85.2, 85.6, 85.6, 86, 86.3, 87.7	(1935)	76.4,
Stanford University School of Medicine.....(1938)	85, 86.3, 86.3	(1938)	82.9,
University of California Medical School... (1937)	82.2, 84.7, 85.6, 85.8	(1937)	76.1,
University of Southern California School of Medicine... (1938)	78.2, 78.6, 79.7, 79.9, 83.3, 84.4, 84.4, 84.6, 84.7, 84.8, 84.9, 85.2, 85.6, 85.9, 86.3, 86.4, 86.8, 86.9, 87, 87.2, 87.6, 87.6, 87.8, 88.7, 89.2	(1938)	77.1,
George Washington University School of Medicine.....(1937)		(1937)	79.9
Georgetown University School of Medicine.....(1937)		(1937)	77.2
Loyola University School of Medicine.....(1930)		(1930)	80.2,
(1938) 80.2, 83.9		(1938)	85.2,
Northwestern University Medical School.....(1937)		(1937)	85.2,
(1938) 81.7, 82.8		(1938)	77, 86.2
Rush Medical College.....(1937)		(1937)	80.7,
University of Illinois College of Medicine.....(1938)		(1938)	82, 82.7, 85.7
State University of Iowa College of Medicine.....(1932)		(1932)	83.8
University of Kansas School of Medicine.....(1937)		(1937)	77.4
University of Louisville School.....(1938)		(1938)	79.3
Tulane University of Louisiana.....(1937)		(1937)	77.8
Harvard University Medical School.....(1936)		(1936)	86.4
University of Michigan Medical School.....(1938)		(1938)	78.9
Wayne University College of.....(1937)		(1937)	81.8
St. Louis University School of.....(1938)		(1938)	80.1, 81.8
Creighton University School of.....(1937)		(1937)	83.7
University of Nebraska College.....(1936)		(1936)	78.4
Woman's Medical College of Pennsylvania.....(1937)		(1937)	87.4
Vanderbilt University School of Medicine.....(1937)		(1937)	81.3, 84.9
Baylor University College of Medicine.....(1937)		(1937)	77.9, 81.6, 84.1
McGill University Faculty of Medicine.....(1932)		(1932)	80
Deutsche Universität Medizinische Fakultät, Prag.....(1932)		(1932)	80

Université de Paris Faculté de Médecine.....(1929)	77.9
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin.....(1920) 78.9, (1926)	84.8
Hessische Ludwigs-Universität Medizinische Fakultät, Gießen.....(1927)	78.8
Thüringische Landesuniversität Medizinische Fakultät, Jena.....(1920)	82.2

School	FAILED	Year Grad.	Per Cent
Stanford University School of Medicine.....(1936)		(1936)	63.3
Northwestern University Medical School.....(1938)		(1938)	70.7
Creighton University School of Medicine.....(1936) 66.6, (1937)		(1936)	74.4
University of Nebraska College of Medicine.....(1935)		(1935)	72.1
Duke University School of Medicine.....(1936)		(1936)	74.2
University of Oklahoma School of Medicine.....(1937)		(1937)	67.8
Universität Köln Medizinische Fakultät.....(1921)		(1921)	70.7

### Indiana June Examination

Dr. J. W. Bowers, secretary, Indiana State Board of Medical Registration and Examination, reports the written examination held at Indianapolis, June 22-24, 1938. The examination covered fifteen subjects and included 100 questions. An average of 75 per cent was required to pass. One hundred and nine candidates were examined, 108 of whom passed and one failed. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
Loyola University School of Medicine.....(1938, 2)*		(1938, 2)	2
Northwestern University Medical School.....(1938, 2)		(1938, 2)	2
Rush Medical College.....(1937), (1938)		(1937), (1938)	2
School of Med. of the Division of Biological Sciences.....(1937)		(1937)	1
University of Illinois College of Medicine.....(1938, 3)		(1938, 3)	3
Indiana University School of Medicine... (1937), (1938, 77)		(1937), (1938, 77)	78
Indiana University School of Medicine.....(1938, 2)		(1938, 2)	4†
University of Louisville School of Medicine.....(1938, 2)		(1938, 2)	2
Johns Hopkins University School of Medicine... (1935), (1938)		(1935), (1938)	2
Harvard University Medical School.....(1937)		(1937)	1
University of Minnesota Med.....(1937)		(1937)	1
St. Louis University School.....(1937)		(1937)	1
Jefferson Medical College of Philadelphia.....(1933)		(1933)	1
McGill University Faculty of Medicine.....(1934), (1938)		(1934), (1938)	2
Albertus-Universität Medizinische Fakultät, Königsberg.....(1925)		(1925)	1
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin.....(1934), (1937)		(1934), (1937)	2
Ludwig-Maximilians-Universität Medizinische Fakultät, München.....(1936)		(1936)	1
Universität Heidelberg Medizinische Fakultät.....(1914)		(1914)	1
Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest.....(1926)		(1926)	1

School	FAILED	Year Grad.	Number Failed
Rheinische Friedrich-Wilhelms-Universität Medizinische Fakultät, Bonn.....(1937)		(1937)	1

\* These applicants have completed the medical course and will receive the M.D. degree on completion of internship. Licenses have not been issued.

† These applicants will be granted licenses on presentation of diploma.

### Nevada Reciprocity Report

Dr. John E. Worden, secretary, Nevada State Board of Medical Examiners, reports three physicians licensed by reciprocity after an oral examination on Aug. 1, 1938. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Kentucky School of Medicine.....(1902)		(1902)	Montana
University of Minnesota Medical School.....(1938)		(1938)	Minnesota
University of Buffalo School of Medicine.....(1918)		(1918)	New York

### New Mexico October Report

Dr. Le Grand Ward, secretary, New Mexico State Board of Medical Examiners, reports the written examination held at Santa Fe, Oct. 10-11, 1938. The examination covered thirteen subjects and included ninety questions. An average of 70 per cent was required to pass. One candidate was examined and passed. Fourteen physicians were licensed by endorsement from August 29 through November 3. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Rush Medical College.....(1937)		(1937)	90.3

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical.....(1916)		(1916)	California
University of Colorado.....(1934) N. B. M. Ex.		(1934)	N. B. M. Ex.
Emory University.....(1930)		(1930)	Florida
Chicago Medical.....(1935)		(1935)	Illinois
University of.....(1936)		(1936)	Kansas
University of.....(1919)		(1919)	Kentucky
University of Louisville School of Medicine.....(1924)		(1924)	Kentucky
Nebraska School of Medicine.....(1899)		(1899)	Wyoming
University of Buffalo School of Medicine.....(1934) N. B. M. Ex.		(1934)	N. B. M. Ex.
Baylor University College of Medicine.....(1933)		(1933)	Texas
University of Texas School of Medicine.....(1937, 2)		(1937, 2)	Texas
University of Wisconsin Medical School.....(1929)		(1929)	Wisconsin

## Book Notices

**The Heart in Pregnancy.** By Julius Jensen, Ph.D. (in Medicine), M.R.C.S., L.R.C.P., Assistant Professor of Clinical Medicine, Washington University School of Medicine, St. Louis. Cloth. Price, \$5.50. Pp. 371, with 5 illustrations. St. Louis: C. V. Mosby Company, 1938.

This volume represents a critical survey of the literature and present day thought on heart disease and its relation to problems of reproduction. Cardiac disease is probably the most frequent accidental complication of pregnancy and accounts for about 7 per cent of maternal deaths. Improved antepartum care has greatly reduced the death rate. The improved prognosis for the patient with cardiac disease during pregnancy has been made possible by cooperative study and care of the patient by a competent internist and an obstetrician. The author, who is an internist, has had the exceptional opportunity of studying a large group of patients with cardiac disease in cooperation with the obstetrician of a prominent American clinic. The first few chapters of this book are devoted to a discussion of the physiology of the heart and circulation in their relation to menstruation, pregnancy and labor. The various cardiac complications are thoroughly discussed. The management of a patient with heart disease in pregnancy and labor is considered. One can take little exception to these general considerations. Some of the rare conditions, such as congenital heart disease and bacterial endocarditis, are accorded more space than their rare occurrence deserves, but there is so little information concerning these conditions in textbooks and periodicals that these thorough discussions are highly desirable. In the author's discussion of the interruption of pregnancy for cardiac disease, he says that "it should now rarely be performed, for either a woman should not undertake pregnancy or she should be capable of carrying it through." This summarizes the value of preconceptional examination for the prospective mother. The volume represents a diligent survey of more than 1,000 references. A great amount of statistical data is thoroughly analyzed. These, plus the experiences of the author, provide an excellent outline of the heart in pregnancy. The work is a real contribution and can be heartily recommended to the obstetrician and the student of the problems of human reproduction.

**Digrafía: Nuevo método radiográfico para el estudio de los órganos móviles.** Por Guido Pollitzer. Paper. Pp. 104, with 41 illustrations. Buenos Aires: Imprenta amorrotu, 1937.

The author recognizes that probably the best method generally available for the study of the movement of organs is fluoroscopy, but even the most carefully made notes and the most tenacious visual memory will not permit comparisons of observations at different times. Stereoscopy does not serve the purpose. Radiocinematography is too expensive, both for the initial outlay for apparatus and for maintenance. Radiokymography has its disadvantages and is more expensive than the simple apparatus required for the author's method. A roentgenkymogram is a roentgenogram of an organ in movement obtained during a prolonged exposure. The "digram" (the author's term) is the production of instantaneous roentgenograms of an organ "surprised" in different positions. The roentgenkymogram registers all the movement, while the "digram" registers only the predetermined positions. The roentgenkymogram in spite of all these considerations gives a blurred image except on its borders, while the "digram" gives a clear image. The roentgenkymogram permits observations of only a small part of the detail of the image of the organ. The "digram" shows 50 per cent or at least one third of the organ. The "digram" is obtained by a frame superimposed on a cassette. In the frame is a grid having bars 3 mm. wide, separated by spaces exactly 3 mm. wide. Thus half the film is exposed when the grid is in one position. The grid is then changed and the half previously exposed is now covered and the other half now uncovered is exposed. A special viewing box permits one to see alternately the first and the second exposures at a slow or rapid rate, as may be desired. This method of viewing gives the illusion of a cinematographic record of movement. As a matter of fact, it is comparable to the commonly seen advertising signs where by a series of parallel shutters one may see first one sign and then another as the turning of the multiple parallel shutters alternately shows the

one or the other. The "digraph" does not compete at all with the roentgenkymograph. It serves another purpose. The roentgenkymograph has had its chief value in recording the amplitude of the movements of the heart and in similar somewhat related studies, whereas the "digraph" will have considerable usefulness in recording and graphically reproducing such lesions as pleuro-pericardial adhesions, adhesions of the diaphragm, chest or the mediastinum, such as accompany nonopaque foreign bodies in the bronchus. The apparatus is not yet made in the United States but it should not be very expensive.

**Chronic Intestinal Toxemia and Its Treatment with Special Reference to Colonic Therapy.** By James W. Wiltzie, A.B., M.D., Consultant in Physical Therapy at the Binghamton City Hospital, Binghamton, N. Y. Cloth. Price, \$3. Pp. 268, with 8 illustrations. Baltimore: William Wood & Company, 1938.

This is an earnest plea for the greater use of colonic irrigations. It is written by a physician who evidently is intelligent, earnest and thoroughly convinced of the value of the method. He starts out with somewhat of an inferiority complex, realizing fully that the medical profession has little faith in his hobby. It has no faith because it has been trying the method at intervals ever since the pyramids were built, and after each flare-up of favor it has watched the idea of intestinal intoxication die down again.

Today the principal users of the method are laymen, cultists and out-and-out charlatans. Obviously, any physician who hopes to overcome this handicap and convince the profession that it should again start washing colons must bring forward a large mass of well documented information. He must show that he is well educated, logical and thoroughly scientific in his presentation and weighing of evidence. His published case reports must show much clinical good sense, and perhaps most important of all, if he is going to convince unbelievers, he must face squarely and explain away all the evidence which they might bring against him. Side-stepping and sneering will not help.

Although this is probably the best written argument for the theory of chronic intestinal toxemia that has yet appeared, it still falls far short of being convincing and satisfying. Although there is much that seems scientific and clinically sound, there is also much that seems like pseudoscience.

One of the most curious features of the book is the author's insistence that the benefits of colonic lavage do not result from the emptying of the bowel but from some remarkable effect in "promoting tubular and cellular drainage, the healing of diseased tissues, the restoration of normal colon function, the improvement of both capillary and lymphatic circulation, and of liver function. The principle back of free drainage is that infection tends to disappear when drainage is adequate, and in the absence of a feeder."

It is startling also to find the use of enemas strongly deprecated as a most pernicious habit which under no circumstances should be started. According to Wiltzie the use of enemas by the patient himself actually tends to undo all the beneficial work that is accomplished by the colon washer in his office. Under such circumstances one should expect to find an exact and detailed explanation of the differences between an enema and an irrigation, but this we have not been able to find in the book.

One thing that will tend much to discourage the scientifically trained physician is the refusal of the author to face the large array of facts which are not favorable to his theory. These are hardly mentioned and, like most enthusiasts, the writer is inclined to quote only that scripture which is to his purpose. The well known fact that in many cases the symptoms of supposed autointoxication are produced reflexly by a distention of the rectum (as shown by the fact that relief comes immediately after defecation) is dismissed rather contemptuously.

It appears then that, although the book will be an excellent text for those who believe in colonic irrigations, it is not sufficiently convincing to induce a trained clinician or gastroenterologist to put a special table into his office and to start off trying to cure all sorts of diseases with this method.

Incidentally, one of the worst defects of the book is that the reader is left with doubts as to what are the indications for the use of this method. At least we are left with the idea that the essential point is to treat the patient with colonic washings, and then if he gets better, one can conclude that he was suffer-



ing from colonic toxemia. The physician who is at all philosophical and logical in his thinking always distrusts this type of argument, if only because with it one can go far to prove that faith healing and spine cracking are excellent modes of healing.

*Die natürliche Heilweise im Rahmen der Gesamtmedizin. Eine Vortragsreihe, veranstaltet von der Berliner Akademie für ärztliche Fortbildung, Berlin NW 7, Robert-Koch-Platz 7. Herausgegeben von Professor Dr. Curt Adam, Leiter der Berliner Akademie für ärztliche Fortbildung. Paper. Price, 14 marks. Pp. 354, with 43 illustrations. Jena: Gustav Fischer, 1938.*

This collection of postgraduate lectures for physicians is symptomatic of modern Germany. Its avowed purpose is that underlying the "new German healing art": the aim to secure a synthesis of scientific medicine with "folk medicine," even though scientific medicine is, after all, the daughter of "folk medicine." It has happened here, as it does in families, that the daughter has lost the appreciation of the wisdom of the mother, while the latter does not understand her daughter any more. It is the sick who suffer therefor, especially those patients for whom the "nature remedies" are prescribed. There is nothing radically different, however, in this series of addresses by various lecturers from the trends of pre-Nazi Germany in the extolling of the value of physical and dietetic remedies: an emphasis that, in this country, which has a tendency to neglect these therapeutic measures, is even more needed than it is in Germany. Unfortunately, the "synthesis" to be effected is with "homeopathy" and most especially "nature cure" empiricism without subjecting these to the strictures of scientific weighing and measuring and to emphasize the "immeasurable" as justification for doing this.

*Injection Treatment of Varicose Veins and Hemorrhoids. By H. O. McPheeters, M.D., F.A.C.S., Attending Physician, New Ashbury, Fairview and Northwestern Hospitals, Minneapolis, Minn., and James Kerr Anderson, M.D., F.A.C.S., Instructor in Surgery, University of Minnesota School of Medicine, Minneapolis. Cloth. Price, \$4.50. Pp. 315, with 82 illustrations. Philadelphia: F. A. Davis Company, 1938.*

This well written compact volume represents an authoritative and practical treatise. It is remarkably complete and yet brief enough to appeal to the busy practitioner. The chapters on anatomy and embryology as well as the other sections on the theoretical considerations of these subjects are excellent. The treatment of varicose veins and the complicating varicose ulcers is described in clear language based on the actual large experience of the authors. All the latest developments are considered and explained in simple language. Considering the voluminous literature that has appeared in recent years and the many controversial points in theory and technic that have been advanced, it is a relief to read a clear exposition which makes available a practical technic based on the best modern conceptions of these subjects. The section on the treatment of hemorrhoids by the injection method, which has been written by Dr. Anderson, is likewise noteworthy for its brevity and condensation into a practical monograph of the voluminous literature on this small but important subject to the general practitioner. The volume represents a type of medical textbook which is too infrequently published, a compact yet detailed practical handbook written in simple direct language containing the best of the latest in the treatment of varicose veins and hemorrhoids.

*Neue biometrische Untersuchungen von Spermien und Fertilität. Von Dr. med. et phil. Konstantin D. J. Generales, jun. Paper. Price, 7 marks. Pp. 84, with 17 illustrations. Stuttgart: Ferdinand Enke, 1938.*

It is now well recognized that in the clinical study of sterility in mated pairs of human beings a thorough examination of the male partner's semen is obligatory, and particularly a study of the morphologic and physiologic characteristics of the spermatozoa. There is also a growing recognition of the fact that detailed investigation of the individual germ cells may possibly be illuminating in cases of genetically grounded diseases and defects. This book is a useful contribution to the methodology of this field of inquiry. In addition to detailed instructions regarding the fixing, staining and measuring of sperm samples, elementary biometric techniques are explained and exemplified. The author's own studies of individual variation in spermatozoa embodied in this book are based on the examination of more than 20,000 sperms. As strictly biometric indexes of quality (in the sense of fertilizing power) of spermatozoa, chief depen-

dence is placed on (a) the product of the coefficients of variation for length and breadth of the sperm head, (b) the coefficient of variation for the volume of the sperm head, which however is not directly measured but is a derivative function of head length and breadth, and (c) the relation between the coefficients of variation for sperm head length and breadth in respect of their absolute magnitudes (fertilizing power being alleged to be diminished when  $C_1 - C_2 > 1$ ). We incline to the view that most critical biometricians would be less trustful of the diagnostic indications derived from coefficients of variation than the author is. The mathematical structure of that constant has made most workers wary about putting too heavy a burden of interpretation on it. The book is clearly written and, even though probably not the final and definitive word on the subject, will certainly help toward its further scientific development.

*A Text-Book of X-Ray Diagnosis. By British Authors. Edited by S. Cochrane Shanks, M.D., Physician, with Charge of Out-Patients, Departments of Radiology and Electro-Therapy, Charing Cross Hospital, London, Peter Kerley, M.D., M.R.C.P., D.M.R.E., Physician to the X-Ray Department, Westminster Hospital, London, and E. W. Twining, M.R.C.S., L.R.C.P., D.M.R.E., Radiologist, Royal Infirmary, Manchester. In three volumes. Volumes I and II. Cloth. Price, 50s; 42s. Pp. 591, with 393 illustrations; 458, with 307 illustrations. London: H. K. Lewis & Co., Ltd., 1938.*

A comprehensive survey of the field of x-ray diagnosis sufficiently detailed for reference purposes and with an adequate bibliography has not been available heretofore in one publication in the English language. This work, projected in three volumes by a group of authoritative English radiologists and clinicians, attempts to fulfil this need. Although it does not measure up in all respects to its foreign language counterparts, the general plan is admirable. In each section are brief discussions of the normal anatomy, the pathology and the chief clinical features of the disease under consideration. This is followed by the roentgenologic features of the condition, occasional discussions of differential diagnosis and a reasonably adequate bibliography. X-ray technic is discussed only as it relates to strictly medical procedures. There is no general introduction to the subject of x-ray diagnosis, no effort at exposition of broad principles nor any other correlative material. The first volume contains a section on the cardiovascular system by Kerley which is only fairly well done. All the information is sound and it is easily read. The illustrations are too few and the subject is insufficiently detailed. X-ray examination of the peripheral vessels is also covered in this section. The second section, on the respiratory tract, by Twining, is excellent. The discussion of fluoroscopic technic and general principles underlying the examination of the lungs is particularly good. The author describes in some detail his simple method of tomography and its application to pulmonary diagnosis. The final section, on the urogenital tract, by Marshall and Shanks, is well presented.

The second volume contains a section on the alimentary canal by Shanks. Gastric ulcer and postoperative gastric conditions are both splendidly detailed. In other respects, however, this section is disappointing. There is little attention to differential diagnosis and the illustrations are clearly insufficient. No reproductions of esophageal varices, gastrojejunocolic fistula or bezoars of the stomach, to mention a few, are given. The section on the biliary tract, by Kerley, is well written with a sufficiency of detail. His account of the appearances in biliary dyskinesia is of particular interest. There is, in addition, in this volume a fairly good discussion of the abdomen, in general, by Shanks and an excellent section on the roentgenologic aspects of obstetrics and gynecology by Roberts and Wilson. The third volume, on the bones and joints and the nervous system, has not yet been published.

There is throughout a regrettable absence of any reference to accuracy or dependability of the x-ray examination. For example, in the detailed and otherwise satisfactory discussion of miliary tuberculosis there is no mention of the fact that weeks may occasionally pass before the roentgenologic aspects of this condition become apparent. It is strange to find so little reference to pneumoperitoneum, which is covered only in relation to gynecology. In the discussion on intestinal obstruction, an extremely important indication for roentgenographic study, the information is most inadequate. There is no reference whatever to retroperitoneal or paraduodenal hernia. American roentgenologists will certainly not agree that filling of the terminal

ileum during examination of the colon is an "undesirable accident." Aside from this, however, there are few statements to which exception can be taken. The bibliography is fairly good but is somewhat marred by glaring typographical errors, such as Schwick for Swick, Davies for Davis, and Chester for Stewart. It is almost incredible that the bibliography of a section on the stomach and duodenum should have omitted all reference to the work of Lewis Gregory Cole. The illustrations, less than 400 for each volume, are too few for a reference book. They are, with few exceptions, reproduced as positives. The printing and figuring are of satisfactory quality. The too few diagrams and elaborately labeled illustrations are excellent.

Despite many deficiencies, these volumes represent an important effort to correct a serious deficiency in our literature. The whole work will no doubt form an indispensable part of every roentgenologist's library and will prove of great value to all who need authoritative reference to the details of x-ray diagnosis.

**The Single Woman and Her Emotional Problems.** By Laura Hutton, B.A., M.R.C.S., L.R.C.P. With a foreword by David Forsyth, M.D., F.R.C.P. Second edition. Cloth. Price, \$1.50. Pp. 173. Baltimore: William Wood & Company, 1937.

This small volume, by an English woman physician, is written for laymen, more particularly for single women. It is a book, however, that can be read with profit by most physicians as well. The author briefly reviews the position of the single woman today. The problem of the single woman has become a more pressing one in countries involved in the World War, since the potential mates of many thousands of women were killed. The modern psychology, emanating chiefly from Sigmund Freud, that offers the basis on which the author discusses her thesis is skilfully if necessarily incompletely outlined. The psychologic problems of friendships among women, sexual problems and sexual inversion are dealt with. Dr. Hutton approaches her thesis not from the standpoint of psychopathology but rather as the problems ordinary women subjected to the special tensions and difficulties associated with a lonely or at least a manless existence are faced with. Her treatment of these problems is sympathetic, humane and scientifically sound. The book can well be read by most intelligent women who face the prospect of a life without marriage.

**Studien über die Entstehung und Entwicklung der Lungentuberkulose mit besonderer Berücksichtigung des Verlaufs der tuberkulösen Erstinfektion des Jugendlichen und Erwachsenen.** Von Hagvin Malmros und Erik Hedvall. Unter Mitwirkung der Röntgendiagnostischen Abteilung (Chefarzt: Dozent H. Hellmer) des Universitätskrankenhauses zu Lund. Nr. 68, Tuberkulose-Bibliothek, Beihefte zur Zeitschrift für Tuberkulose. Herausgegeben von Dr. Franz Redeker, Oberregierungs- u. Obermedizinalrat, Berlin, und Dr. Karl Diehl, dirigierender Arzt, Sommerfeld. Paper. Price, 27 marks. Pp. 223, with 140 illustrations. Leipzig: Johann Ambrosius Barth, 1938.

Periodic study with tuberculin test and x-ray examination of more than 3,000 young men and women at the University of Lund in southern Sweden permitted the authors to observe the development of pulmonary lesions in 133 students. Their observations dealing with the genesis of tuberculosis are of great importance. The studies were carried out with thoroughness and the results are reported in detail. Only rarely was the "subclavicular infiltrate" found to be the earliest lesion. As a rule the initial manifestation of pulmonary tuberculosis was above the clavicle, indicated by discrete soft spots in the x-ray film. Spread below the clavicle was usually followed by confluence of the spots, simulating a primary exudative infiltrate. Apical infiltrations of this sort were frequently noted, without evidence of a primary complex, in students who had only recently become tuberculin positive. Apical lesions progressed to clinical disease and occasionally to death, with equal frequency in students recently infected and in those long positive to tuberculin. The authors warn that apical or subapical lesions must be considered serious even when they are believed to be of first infection type. Illustrative roentgenograms, reproduced with remarkable clarity, greatly enhance the value of this report. The progression of tuberculosis from minute apical infiltrations to advanced disease can be plainly followed in these excellent reproductions. This volume will prove of exceptional value to physicians interested in the pathogenesis of tuberculosis and will be highly useful to roentgenologists, who will find it a comprehensive atlas of the early lesions of pulmonary tuberculosis.

**Practical Otolaryngology.** By Morris Levine, M.D., F.I.C.S., Clinical Professor of Otolaryngology, New York Post-Graduate Medical School, Columbia University, New York. Second edition. Cloth. Price, \$5.50. Pp. 416, with 149 illustrations. Philadelphia: Lea & Febiger, 1938.

This popular small book on diseases of the ear consists essentially of a compilation of lectures given by the author for the New York Post-Graduate Medical School of Columbia University. The book is short and concise, written in an easily readable style. There is not much detail or theory, which the author defends in his preface for reasons which appear good to him. Hence, though it is an excellent book for medical students, general practitioners and perhaps those starting the practice of otology, it is not complete enough for the practicing specialist. The descriptions of disease are good. The chapters on acute otitis media and mastoiditis are among the best in the book and are worthy of praise. There is an excellent chapter on petrositis which summarizes most of the new thought on this subject. If there is any criticism of the book it lies in the preliminary chapters. In spite of the fact that the author prefers not to consume too much space in the discussion of theories and debatable points, it does not seem altogether fitting that a book published in 1938 should omit those newer studies of otology pioneered by Wever, Bray and others, and which have given such impetus to theory and practice in recent years.

**Comparative Study of the Marmas.** By P. V. Krishna Rao, B.A., M.B., B.S., Professor of Physiology and Hygiene, Govt. Indian Medical School, Madras. Cloth. Price, 5s. Pp. 68, with illustrations. Madras: P. Varadachary & Co., 1937.

The word Marma is derived from the Sanskrit root "Mru," "Marane" and it applies to a place of vital importance in the body which, if injured, results in serious consequences or death sooner or later. Surgeons of ancient India laid down the rule that in a case of surgical operation the situation and the dimension of each local marma should first be studied well and the incision for operation made in such a way as to avoid even the edge of a marma. The knowledge of the marmas was made use of in ancient warfare and in hunting after wild animals by aiming at the marmas with the arrows. This science is also practiced in the art of wrestling in some parts of India and Japan. The author has extracted the relevant passages from Hindu Scriptures and translated them into English. He describes, in the light of modern anatomy, the structure of each "marma" with its corresponding anatomic parts, with their names according to the western system. The author then prescribes medicines and methods of treatment for disorders of each affected "marma." These are derived from his own private practice and not from any standard Hindu works. It is doubtful whether modern medicine would approve this part of the book. The "marmas" themselves are still authentic.

**Personal Hygiene.** Compiled by Robert Olesen, Assistant Surgeon General, United States Public Health Service. Supplement No. 137 to the Public Health Reports. U. S. Treasury Department, Public Health Service. Paper. Price, 10 cents. Pp. 46, with illustrations. Washington, D. C.: Supt. of Doc., Government Printing Office, 1938.

Health maintenance is largely a personal responsibility. This short compilation of information concerning personal hygiene, originally prepared for radio use, has been revised and brought down to date. Cleanliness, immunization against infectious diseases, school hygiene, food, posture, sport, care of the hair and scalp, and first aid are among the subjects briefly but clearly discussed. A short bibliography is appended. This booklet serves as a useful guide to a few of the phases of personal hygiene.

**A Manual of Tuberculosis for Nurses and Public Health Workers.** By E. Ashworth Underwood, M.A., B.Sc., M.D., Medical Officer of Health, County Borough of West Ham. With an Introduction by Professor J. R. Currie, M.A., M.D., F.R.C.P., Professor of Public Health in the University of Glasgow. Second edition. Cloth. Price, \$3.25. Pp. 401, with 53 illustrations. Baltimore: William Wood & Company, 1938.

For nurses on duty with tuberculous patients this book is excellent. The manner of infection and description of primary and secondary types are well handled. The description of symptoms, what produces them and what a nurse might do is carefully explained. Sanatorium care, together with an explanation of what is to be expected from such treatment, is given in detail. All a nurse should know about the surgery of all forms

of tuberculosis is set forth. From the point of view of the public health worker and preventive medicine the book is not all inclusive. This phase of tuberculosis is not presented in sufficient detail. Had the title omitted "public health workers" the work would accomplish its purpose.

Berättelse från styrelsen för cancerföreningen i Stockholm över verksamhetsåret 1937. Index of Papers Published at Radiumhemmet 1909-1937. Report on Cases Treated at Radiumhemmet 1921-1937. Paper. Pp. 103. Stockholm: K. L. Beckmans Boktryckeri, 1938.

The list of papers contains 287 titles. The tabular summary of the results of treatment covers 55,038 cases grouped under 879 different disease conditions. Any details of treatment are not given.

## Bureau of Legal Medicine and Legislation

### MEDICOLEGAL ABSTRACTS

**Workmen's Compensation Acts: Recovery Retarded by Mental Sequelae of Industrial Injury.**—Vallee had a spinal malformation and chronic bronchitis. In the course of his employment, April 3, 1936, four of his ribs were fractured, one rib piercing a lung. His employer paid him full compensation from April 3 to Oct. 12, 1936, and thereafter refused to pay him anything. In a proceeding instituted under the workmen's compensation act, the trial court awarded the workman compensation on the basis of total disability to April 3, 1938, and of partial disability from then to April 3, 1940. The employer thereupon brought exceptions to the Supreme Court of New Hampshire.

The employer's argument, said the court, is substantially fallacious in its insistence that the direct consequences of the accident are limited to the immediate consequences. Any aggravation of the claimant's spinal malformation or of the bronchitis, by the accident or the consequences thereof, was properly attributed to the accident. Furthermore, the mind, as well as the body, may be hurt by a traumatic injury. If conditions arising in the course of recovery affect the mind in such a way as to retard convalescence, the resulting prolongation of disability may be attributed to the accident. Loss of work and of bodily strength and activity may cause depression or melancholy which, even though mild, may prolong disability.

The defendant's medical expert testified that the plaintiff's condition was partly due to his injury, that some soreness from the broken ribs persisted and greatly worried him, and that he was suffering from "a mental condition to a large extent which started at the time of the accident." This mental condition, the witness testified, accounted for the workman's feelings of weakness and loss of strength whenever he tried to do any work. He further testified that the workman's complaints of backache were due to the long time he had been out of work, his apprehensions about himself, the long period of sitting around and disuse of his back muscles, so that they had become soft and weak. This evidence, the court said, together with that tending to show that before the accident the workman worked steadily while thereafter he was unable to work except to a negligible extent, that his general health was poor after the accident, that he lost 15 pounds in weight and became anemic, that he had severe back pains and that his complaints were not of pretended suffering, was sufficient to support the findings of the trial court. Although the workman's back was not hurt in the accident, the court thought it reasonable to infer that inactivity due to the accident brought about some condition in connection with his spinal deformity which caused suffering from it, and although his chronic bronchitis was progressive as time went on, it was a fair deduction that the accident developed and increased the speed of its progress.

After reviewing carefully the entire record, the Supreme Court was of the opinion that the award of compensation made by the trial court to the workman was justified.—*Tallice v. Spaulding Fibre Co. (N. H.)*, 197 A. 697.

**Optometry Practice Acts: Revocation of Optometrist's License Because of Corporate Employer's Use of Prohibited Advertising.**—The Minnesota optometry practice act authorizes the state board of optometry, after notice and hearing, to revoke the license of any licensee found guilty of conduct of a character likely to deceive or defraud the public, including such practices as price advertising, advertising free examinations, splitting fees or the use of untruthful, improbable, misleading or impossible statements in connection with practice or treatment. The act authorizes the board to make any rules and regulations, not inconsistent with law, which it may deem necessary for the effective enforcement of the act. The board undertook, by rule 6, to declare that unprofessional conduct would be imputed to a licensed optometrist employed by a firm or corporation if his employer engaged in any advertising prohibited by law or board rule. The plaintiff, a licensed optometrist, was charged, in a revocation proceedings, with being in the employ of a jewelry company that used types of prohibited advertising, that he, the plaintiff, aided and abetted his employer in doing so, and that he was therefore guilty of unprofessional conduct. The district court, Ramsey County, at the instance of the plaintiff, enjoined the board from revoking the plaintiff's license, and the board appealed to the Supreme Court of Minnesota.

In the opinion of the Supreme Court, the board was without power to revoke the plaintiff's license under the circumstances stated. Since the optometry practice act, said the court, provides that unlicensed persons may sell optometric articles if such sale is under the control and direction of a licensed optometrist who is in charge of and in personal attendance at the place where such articles are sold, clearly it is lawful for a licensed optometrist to accept such employment. The employment being lawful, it seemed to the court to be contrary to the letter and spirit of the law to hold the employee responsible for the employer's violation of the law and to impute knowledge of such violations to the employee. If the employer violates the act in any manner, he may be enjoined or prosecuted. There is no right or justice in punishing the servant for the misdeeds of the master. The court did not overlook the fact that the complaint filed with the board charged that the plaintiff aided and abetted his employer, but the court thought that it was clearly evident from a reading of the complaint as a whole that that allegation was a conclusion drawn from the fact that the plaintiff did not quit the employment when informed of the employer's transgressions.

The primary purpose of optometry legislation, continued the court, is the protection of human eyesight. Such legislation was not enacted to further the personal interests of the optometrists except so far as their advancement in skill and efficiency serves the primary purpose of the law. When the purchaser of eyeglasses has the services of a competent licensed optometrist in selecting and fitting them to his eyes, he has had all the benefits the law intended.

The Supreme Court accordingly affirmed the judgment of the trial court enjoining the board from revoking the plaintiff's license.—*Williams v. Mack (Minn.)*, 278 N. W. 585.

## Society Proceedings

### COMING MEETINGS

- American Academy of Orthopedic Surgeons, Memphis, Tenn., Jan. 15-19.
- Dr. Carl E. Badgley, 1313 East Ann St., Ann Arbor, Mich., Secretary.
- American Association for the Study of Neoplastic Diseases, Baltimore, Dec. 28-30. Dr. Eugene R. Whitmore, 2139 Wyoming Avenue N.W., Washington, D. C., Secretary.
- American Student Health Association, New York, Dec. 29-30. Dr. Ruth E. Boynton, Students Health Service, University of Minnesota, Minneapolis, Secretary.
- Eastern Section, American Laryngological, Rhinological and Otological Society, Boston, Jan. 11. Dr. Frank E. Kittredge, Masonic Temple, Nashua, N. H., Chairman.
- Middle Section, American Laryngological, Rhinological and Otological Society, Sioux City, Iowa, Jan. 19-20. T. R. Gittins, Davidson Bldg., Sioux City, Iowa, Chairman.
- Southern Section, American Laryngological, Rhinological and Otological Society, New Orleans, Jan. 14. Dr. Francis E. LeJeune, Maison Blanche, New Orleans, Chairman.
- Western Section, American Laryngological, Rhinological and Otological Society, Spokane, Wash., Jan. 29. Dr. Frederic G. Sprowl, Medical Arts Bldg., Spokane, Wash., Chairman.

## Current Medical Literature

### AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1928 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (\*) are abstracted below.

### American Journal of Medical Jurisprudence, Boston

1:73-144 (Oct.) 1938

- Legal Phases of Psychiatry. A. Myerson, Boston.—p. 73.  
Accidents in Radiology. E. H. Skinner, Kansas City, Mo.—p. 79.  
Validity of Postmortem Tests for Alcoholism. R. E. Cornish, H. D. Draper and J. Finn Jr., Berkeley, Calif.—p. 86.  
Carbon Monoxide Poisoning. W. D. McNally, Chicago.—p. 89.  
The Work of a Medical Examiner's Office: Description of How It Is Accomplished in New York City. B. M. Vance, New York.—p. 95.  
Preliminary Survey of 1,000 Case Histories of Inmates of the Elmira Reformatory. R. Breguet, Elmira, N. Y.—p. 101.  
Medical Testimony. H. E. Mock, Chicago.—p. 119.

### Annals of Surgery, Philadelphia

108:801-960 (Nov.) 1938

- Observations on Mode of Action of Sulfanilamide and Its Application to Surgical Infections. J. S. Lockwood, Philadelphia.—p. 801.  
Toxic Manifestation of Sulfanilamide. P. H. Long and Eleanor A. Bliss, Baltimore.—p. 808.  
Effect of Sulfanilamide on Human, Virulent Hemolytic Streptococci. C. Lyons, with technical assistance of Anita Mangiaracine, Boston.—p. 813.  
Treatment of Hematogenous Nephritis with Sulfanilamide: Case Report. H. H. Young and S. A. Vest, Baltimore.—p. 828.  
Treatment of Intraperitoneal Abscess Arising from Appendicitis. E. P. Lehman and W. H. Parker, University, Va.—p. 833.  
Regional Enteritis. C. F. Dixon, Rochester, Minn.—p. 857.  
Perianal Fistulas as Complication of Regional Ileitis. A. Penner and B. B. Crohn, New York.—p. 867.  
\*Acute Cholecystitis: Results of Operation Within Forty-Eight Hours of Onset of Symptoms. H. F. Graham and M. E. Hoeft, Brooklyn.—p. 874.  
Epidermoid Cysts of the Spleen. A. H. Montgomery, E. T. McEnery, Chicago, and A. A. Frank, Malden, Mass.—p. 877.  
Embryoma of Kidney (Wilms' Tumor). W. E. Ladd, Boston.—p. 885.  
Therapeutic Management of Urinary Infections. A. Randall and B. Hughes, Philadelphia.—p. 903.  
\*Thymol Therapy in Actinomycosis. T. M. Joyce, Portland, Ore.—p. 910.  
\*The Problem of Wound Healing: Effect of Local Antiseptic Agents on Infected Wounds. D. P. Anderson Jr., Philadelphia.—p. 918.  
Effect of Urinary Bladder Transplants and Extracts on Formation of Bone: Further Experimental Study. G. H. Copher, St. Louis.—p. 934.  
Apparent Alteration of Tetanus Toxin Within Spinal Cord of Dogs. W. M. Firor and A. Lamont, Baltimore.—p. 941.

**Acute Cholecystitis.**—Of 167 patients with acute cholecystitis on whom Graham and Hoeft operated within forty-eight hours of the onset, death occurred in six. Cholecystectomy was the operation of choice in these cases, while cholecystostomy was reserved for the more critical ones. Certain factors make a cholecystectomy for acute cholecystitis more difficult than one performed in the quiescent period. The gallbladder is often tense and distended. The tissues are more friable and the bleeding is more profuse. There is more swelling around the cystic duct. It may be necessary to aspirate the gallbladder, and the authors usually prefer in these acute cases to remove it from above downward, controlling the bleeding from the liver bed by the pressure of a gauze pad and a retractor. An oozing liver bed that cannot be obliterated can be quickly peritonealized and rendered dry by a free omental graft lightly tacked in place by a few interrupted sutures. A large percentage of cultures taken during the first forty-eight hours remain sterile and therefore infection is not a major problem at this time. Acute cholecystitis is not like acute appendicitis and there is not the same necessity for prompt operative intervention. But of twenty-seven patients operated on within two to five days of onset two died and of twenty-two operated on five or more days after onset five died. It is seen that a delay of more than five days gives a high operative mortality and raises the question of whether operation should be performed or further delay advised.

This must be decided for each individual case. A lowering in mortality can be accomplished by education of the public and cooperation between the family physician and the surgeon to secure a prompt operation, early in the attack, for every person suffering from acute cholecystitis who is a good operative risk.

**Thymol Therapy in Actinomycosis.**—Joyce believes that the most effective treatment of actinomycosis is a combination of radical surgical intervention and thymol medication. His procedure is to give orally 1.5 Gm. of powdered thymol in capsules two out of every three days, to open the sinuses widely, to curet and fill them with thymol in olive oil (10 per cent solution) and then to inject the sinuses each day. Small strips of gauze are inserted to keep the sinuses open.

**Wound Healing.**—In an attempt to ascertain the exact value of topical agents in the treatment of infected wounds, Anderson measured precisely the changes in the size and bacterial count of twenty wounds. The wounds studied differed in size, etiology and bacterial flora, but each was of the type regarded as surgically infected. The majority of infected wounds, adequately drained and not containing sloughing tissue, in normal persons will heal according to a regular geometric curve, the rate being proportional to the size of the wound and decreasing with the age of the patient, regardless of the type of local treatment. Invasive organisms, extensive necrosis and the presence of dead tissue in the wound, even without active infection, retarded healing. The presence of a large number of organisms on the surface of wounds does not ordinarily retard healing. Local agents considered had little or no beneficial effect on the healing of infected wounds, except for the action of zinc peroxide in specific cases. The few antiseptic agents which had definite bactericidal action on surface organisms in normal granulating wounds were ineffective in the presence of tissue necrosis, and it is only under the latter circumstances that the existing infection is likely to retard healing. In the management of infected wounds, less attention should be given to the selection of a potent local antiseptic agent. It is of more importance to consider the problem of increasing local tissue immunity, which may be influenced by factors of a general nature remote from the site of the wound, and aiding the sequestration of necrotic tissues rich in bacteria by mechanical or chemical débridement and adequate surgical drainage.

### Archives of Ophthalmology, Chicago

20:709-906 (Nov.) 1938

- Implantation of Hollow Grooved Body into Orbit for Filling Late After Enucleation of Eyeball. J. M. Wheeler, New York.—p. 709.  
Determination and Significance of Scotopic Retinal Visibility Curve. E. Ludvig, Boston.—p. 713.  
Physiologic and Clinical Ophthalmologic Problems in Relation to Individual Variability. A. Brückner, Basel, Switzerland.—p. 726.  
Congenital Buphthalmos Complicated by Dislocation of Lens and Hemorrhage into Vitreous with Complete Recovery of Central Vision. W. J. Holmes, Warren, Ohio.—p. 757.  
Circulation of Aqueous: VII. Mechanism of Secretion of Intra-Ocular Fluid. J. S. Friedenwald and R. D. Stiehler, Baltimore.—p. 761.  
Coloboma of Optic Nerve and of Macula: Microscopic Study. D. Wexler and M. Last, New York.—p. 787.  
Acute Alcoholic Amaurosis. F. D. Carroll and R. Goodhart, New York.—p. 797.  
\*Panophthalmitis and Sympathetic Ophthalmia. B. Samuels, New York.—p. 804.  
Experimental Hypertension: VIII. Vascular Changes in the Eyes. J. E. L. Keyes and H. Goldblatt, Cleveland.—p. 812.  
Reading Difficulties in Children. G. E. Berner and Dorothy E. Berner, Philadelphia.—p. 829.  
Carbon Disulfide Poisoning. R. McDonald, Philadelphia.—p. 839.

**Panophthalmitis and Sympathetic Ophthalmia.**—Samuels points out that panophthalmitis is of relatively rare occurrence today, not only because severely injured eyes are excised before the infection is far advanced but because the usual infecting germs do not lead to a widespread purulence. However, in regions with warm climates it is still relatively frequent, whereas in the United States it probably represents not more than 2 or 3 per cent of all intra-ocular infections following injuries. Of 101 globes showing characteristic sympathetic tissue, reported in a previous paper, there were only three which had been affected with panophthalmitis. In this same series there were nine instances of typical sympathetic infiltration of the choroid without involvement of the fellow eye. Of these nine, seven followed common endophthalmitis and two followed panophthal-

mitis. Thus three cases of panophthalmitis in a series of 101 cases of sympathetic ophthalmia is not an insignificant figure and suggests that a panophthalmitic eye may not be so harmless as has been commonly thought.

### Archives of Surgery, Chicago

37: 697-864 (Nov.) 1938

- Ovarian Dysgerminoma. G. E. Seegar, Baltimore.—p. 697.
- \*Infections of the Hand: Three Years' Experience in a Clinic for Study of Whitlow. E. A. Devenish, London, England.—p. 726.
- Treatment of Intestinal Obstruction. J. Bottin, Liège, Belgium.—p. 735.
- Spreading Peritonitis Complicating Acute Perforative Appendicitis: Experimental Studies. J. O. Bower, J. C. Burns and H. A. Mengle, Philadelphia.—p. 751.
- Degeneration of Infundibular Nerve Fibers in the Cat Without Appreciable Polydipsia. A. D. Keller and J. W. Hamilton Jr., University, Ala.—p. 760.
- \*Serum Therapy for Infections with Streptococci: General Observations. Adele E. Sheplar, Martha Jane Spence and W. J. MacNeal, New York.—p. 772.
- Hepatic Damage in Biliary Disease: Its Relation to Concentration of Bile Acids in the Bile. H. K. Gray, J. M. McGowan, W. S. Nettrout and J. L. Bollman, Rochester, Minn.—p. 790.
- Technic of Ivory Implant for Correction of Saddle Nose. M. M. Wolfe, Philadelphia.—p. 800.
- Duodenal Ruptures. A. Lurje, Ivanovo, U. S. S. R.—p. 808.
- \*Maggot Therapy for Hematogenous Osteomyelitis of the Tibia. S. Maddock, with the assistance of Dorothy Jensen, Boston.—p. 811.
- End Results of Tuberculous Cystitis: Report of Cases. J. B. Wear, Madison, Wis.—p. 821.
- Cysts of External Semilunar Cartilage: Report of Three Cases. S. Kleinberg, New York.—p. 827.
- Review of Urologic Surgery. A. J. Scholl, Los Angeles; F. Hinman, San Francisco; A. von Lichtenberg, Budapest, Hungary; A. B. Hepler, Seattle; R. Gutierrez, New York; G. J. Thompson, J. T. Priestley, Rochester, Minn.; E. Wildbolz, Berne, Switzerland, and V. J. O'Connor, Chicago.—p. 835.

**Infections of the Hand.**—Devenish states that during a period of three years 388 patients with infections or injury of the hand were seen at the University College Hospital. There were sixty-one cases of injury, leaving 327 cases of infection (whitlow), in 192 of which there was a history of injury. Of the cases of infection of the digital pulp, of paronychia and of subcutaneous abscess and cellulitis of the fingers, trauma occurred in 64, 50 and 65 per cent, respectively. With the other types of whitlow the figures were not large enough to indicate the significance of trauma. If trivial injury received prompt treatment, the incidence of whitlow was much reduced. Such measures are immediate cleansing of the wound, its protection against contamination and a warning to the patient to report immediately if the lesion becomes painful. At present so much attention is focused on the site of the incision and the necessity for early operation "to relieve tension" that unnecessary operations are apt to be encouraged. Premature incision for spreading cellulitis is by no means a harmless blunder; it may determine the onset of sloughing. It is more difficult to abort an infection of the pulp than to arrest cellulitis elsewhere in the hand, but this is probably due to the situation of the pulp at the end of the arterial tree of the upper limb. Premature incision for cellulitis of the pulp is thus more likely to result in extensive sloughing and may possibly cause necrosis of the terminal phalanx. Swelling and congestion of the inflamed area are reduced to a minimum by elevation of the limb and immobilization. Splinting for immobilization or elevation must not interfere with the circulation. The hand seems to be dependent for efficiency on constant use. Complete disuse, whether produced by therapeutic immobilization or by a tender scar, is followed by atrophic changes in the fingers, which result in their disablement. This may be prevented in the former instance by discontinuing immobilization and by starting active movements as soon as healing is established.

**Serum Therapy for Streptococcal Infections.**—Sheplar and her associates report sixty-six severe cases of streptococcal infection, seen in consultation, treated with concentrated anti-streptococcus serum. The youngest patient was 19 days old and the oldest 80 years. Of the sixty-six patients, eighteen died. There were six patients with diffuse bacterial meningitis and two with generalized peritonitis, types of disease in which the serum at present available does not offer much hope. In only three of the eighteen cases was the effect of the serum really

disappointing. Five successful cases are cited illustrating the use of the serum under varied conditions. The first is an example of temporary invasion of the blood stream from lesions on the hands, treated by subcutaneous injections of concentrated state serum to a total amount of 40,000 units. The patient recovered promptly from the infection. The second patient was desperately ill with streptococcal pneumonia, empyema and bacteremia. She was treated with polyvalent streptococcus serum from February 10 to April 2 and the total amount of serum used was 760 cc.; this treatment was augmented by multiple transfusions and surgical drainage of the pleural cavity. The third patient, with postoperative streptococcal infection, was treated with the regular (unconcentrated) serum of the New York state department of health. The first administration of the serum (25,000 units) on May 16 was followed by improvement. An injection of 5,000 units of the serum was given on May 20. After a period of improvement there were a relapse and extension of the inflammation and on May 29 more serum was given in divided doses, to a total amount of 15,000 units. This was followed by 10,000 units on May 30 and 5,000 units on each of three consecutive days. This time there was prompt improvement without further relapse. The fourth patient had postoperative streptococcal infection. A streptococcus bacteriophage was applied to the wounds and 40,000 units of concentrated streptococcus serum (New York state) was given intramuscularly on each of two days. The last patient was treated with sulfanilamide in moderate doses for four days and with streptococcus serum on these four days and for eight days thereafter. She made a rapid recovery. There was no incompatibility between the serum and sulfanilamide or streptococcus bacteriophage employed simultaneously. There is reason to believe that superior results may be obtained by the careful use of these agents in combination. The authors propose to designate as the Hugh Young reaction the chill, sudden rise in temperature, diaphoresis and fall in temperature so often observed in the treatment of sepsis when an adequate amount of the antibacterial agent has been introduced into the blood stream to initiate the eradication of the infecting bacteria.

**Maggot Therapy for Hematogenous Osteomyelitis.**—Maddock used maggot therapy in the treatment of twenty-nine cases (thirty-one lesions) of hematogenous osteomyelitis of the tibia. Most of the patients had been operated on by other surgeons, and treatment with maggots was begun after a period of antecedent treatment. The great advantage in the use of maggots seems to lie in the high percentage of closed lesions and in the relative scarcity of recurrences. This is doubtless due to the ability of the larvae to uncover hidden sequestrums and to seek out small abscesses which might otherwise become included in the new bone. Maggot therapy is not indicated in all cases of osteomyelitis. Only when the patient fails to make reasonable progress clinically is it necessary to consider the use of maggots. For chronic osteomyelitis their usefulness is probably much greater. After seven years of experience and many trials of various substitutes the author still feels that the condition can be treated profitably with maggots and that no lesion should be given up as hopeless until maggot therapy has been tried. Of the thirty-one lesions, twenty-six up to the time of writing were closed, one still required treatment, two had necessitated amputation and two patients were lost track of.

### Bulletin of Neurol. Inst. of New York, New York

7: 95-210 (Sept.) 1938. Partial Index

- Relapsing Juvenile Chronic Subdural Hematoma: Clinical and Reentgenographic Study. L. M. Davidoff and C. G. Dyke, New York.—p. 95.
- Comparison of Series of Olfactory and Visual Tests for Localization of Tumors of the Brain. C. A. Elsberg and H. Spitzniz, New York.—p. 165.
- Subjective Foveal Hemianopsia During Dark Adaptation in Patients with Tumors of Temporal Lobe. H. Spitzniz, New York.—p. 170.
- Myeloscope: Diagnostic Inspection of Cauda Equina by Means of an Endoscope (Myeloscope). J. L. Pool, New York.—p. 178.
- Comparison of Spinal Fluids in Active and Inactive Cases of Multiple Sclerosis. S. M. Dillenber, New York.—p. 190.
- Comparison of Symptoms of Glioblastoma Multiforme and Fibrillary Astrocytoma of Temporal Lobe. R. T. Collins, New York.—p. 195.
- Laterality of Signs and Symptoms in Series of Pathologically Verified Tumors of the Brain. T. E. Bamford Jr., New York.—p. 201.

# Canadian Medical Association Journal, Montreal

39: 419-516 (Nov.) 1938

- Progress in Ophthalmology. S. Duke-Elder, London, England.—p. 419.  
Rheumatic Fever. J. C. Mcakins, Montreal.—p. 426.  
Unusual Findings in Case of Acute Mercurial Poisoning. I. M. Rabinowitch, Montreal.—p. 429.  
One Hundred Broken Noses. J. W. Gerrie, Montreal.—p. 433.  
Tattooing of the Cornea. J. N. Roy, Montreal.—p. 436.  
Congenital Hernia into Umbilical Cord: Two Cases, One Associated with Persistent Cloaca. C. W. Burns and M. A. Ogryzlo, Winnipeg, Man.—p. 438.  
Calcium Carbonate Deposits in Human Gallbladder. A. T. Cameron, F. D. White and Sara Meltzer, Winnipeg, Man.—p. 441.  
Experimental Production of Peptic Hemorrhagic Esophagitis. H. Selye, Montreal.—p. 447.  
Risk of Spinal Puncture. H. H. Hepburn, Edmonton, Alta.—p. 449.  
\*Facial Paralysis Complicating Mastoid Operations. J. A. Sullivan, Toronto.—p. 451.  
A Résumé on Undulant Fever: Use of Protosil and Prontylin: Report of Two Cases. R. H. Fraser, F. D. White and M. B. Perrin, Winnipeg, Man., with collaboration of Esther B. Hardisty, Vancouver, B. C.—p. 455.  
\*Amyloidosis of Adrenals as Cause of Addison's Disease. D. L. Mendel and M. Saibil, Montreal.—p. 457.  
\*Significance of Low Leukocyte Count in Acute Pyogenic Infections. C. H. Watson and T. R. Sarjeant, Toronto.—p. 460.  
What Report Should a Physician Expect from a Dentist? G. A. Morgan, Toronto.—p. 465.  
Common Errors in Certifying Cause of Death on Medical Certificate. A. H. Sellers, Toronto.—p. 468.

**Facial Paralysis Complicating Mastoid Operations.**—Sullivan bases his conclusions on his reparative operative experiences in sixty cases of facial nerve palsies and anatomic dissections of the temporal bones of animals. 1. The systematic identification of the sigmoid sinus plate, the horizontal canal, the digastric crest, traced forward to the posterior bony canal wall, and the joining together of the latter two structures reveals a plane for the position of the vertical segment. 2. The tympanic segment of the nerve may be injured in the simple mastoid operation. The position of the horizontal canal is fixed, the anterior margin of which is the posterior border of the fallopian aqueduct. Therefore this structure must constantly be observed in opening the mastoid antrum, as in reality it affords a protection to the nerve. 3. In the radical operation the tympanic segment must be visualized. The "bridge," so called, should never be removed by any manipulation directed from the middle ear toward the mastoid antrum. 4. The nerve in sclerotic bone is more superficial on the tympanic aspect of the posterior bony canal wall, the so-called pyramidomastoid segment, and is most prone to injury in the lowering of the hypotympanum and the removal of the bony margin of the annulus tympanicus on this surface. 5. Handled thus, facial paralysis complicating the mastoid operation is on the way toward coming under surgical control, the prognosis, heretofore invariably grave, will give better promise and the malady will be less and less common.

**Amyloidosis of Adrenals as Cause of Addison's Disease.**—Mendel and Saibil present a case of Addison's disease developing on the basis of amyloidosis in the course of pulmonary tuberculosis, with no evidence of tuberculosis in the adrenals, an apparently uncommon occurrence. The adrenals are frequently involved in the course of generalized amyloidosis, yet Addison's disease on this basis is extremely rare. It appears to depend on the degree of amyloid infiltration and the extent of clinical development of the syndrome of Addison's disease.

**Low Leukocyte Count in Pyogenic Infections.**—After determining the leukocyte and polymorphonuclear counts in cases of appendicitis, pneumonia and other pyogenic infections, Watson and Sarjeant believe that the sequence of events in leukocytosis is as follows: 1. During the early stages of a severe pyogenic infection there is a rapid production of leukocytes, which are delivered to the blood as young forms. This causes an increase in the total leukocyte count and a shift to the left in the polymorphonuclear count. 2. The white cell count continues to rise until, with the onset of suppuration, leukocytes are withdrawn from the blood to the infected focus more rapidly than they are poured into the blood from the bone marrow. If the infective process continues to spread, this withdrawal of leukocytes from the circulation may be of sufficient extent to produce leukopenia. The curves of the leukocyte and polymorphonuclear counts in uncomplicated cases of lobar pneumonia are similar to the curves

in uncomplicated cases of acute appendicitis, rising abruptly with the onset of the infection, remaining high during the acute stages of the disease and falling together to the base line as the infection subsides. In cases of lobar pneumonia complicated by empyema, the curves resemble those in acute appendicitis with abscess formation or peritonitis, as with the onset of suppuration in the pleural cavity the leukocyte count shows an abrupt fall while the polymorphonuclear factor remains elevated.

# Connecticut State Medical Society Journal, Hartford

2: 523-590 (Nov.) 1938

- Horace Wells and His Discovery of Anesthesia. W. R. Steiner, Hartford.—p. 525.  
Hypnotism and Its Relation to Anesthesia. B. B. Raginsky, Montreal.—p. 527.  
Postoperative Atelectasis. H. F. Bishop, Hartford.—p. 534.  
\*Some Experiences Gained in Series of 500 Epidural Blocks. B. C. Sword, New Haven, and A. E. Harrington, Milford.—p. 539.  
Methods of Anesthesia for Operations About the Head and Neck. R. C. Adams, Rochester, Minn.—p. 544.  
Present Status of Pentothal Sodium as an Anesthetic Agent. M. Garofalo, Hartford.—p. 550.  
Role of Surgery in Treatment of Heart Disease. H. M. Marvin, New Haven.—p. 558.  
Late Latent Syphilis. A. K. Poole, New Haven.—p. 569.

**Epidural Block.**—From an experience of 500 epidural block anesthetics Sword and Harrington conclude that the procedure can be used in most types of cases in which operation is below the diaphragm. Old age is not a contraindication. In the majority of cases adequate sedation can be produced by the proper timing of the preliminary medication. Too great a fall in blood pressure occurs if morphine, scopolamine or pentobarbital sodium is given in the usual doses an hour before the operation. The main objection to this type of anesthesia seems to be the delay it causes in a busy operating room. Poor surgical risks show a better recovery when this method of anesthesia is used.

# Indiana State Medical Assn. Journal, Indianapolis

31: 593-662 (Nov.) 1938

- Tuberculosis Association and the Problem of Early Diagnosis. M. A. Auerbach, Indianapolis.—p. 594.  
Pulmonary Tuberculosis: The Problem of the General Practitioner. J. V. Pace, Rockville.—p. 596.  
Tuberculosis in General Practice. C. J. McIntyre, Indianapolis.—p. 599.  
Medical Treatment of Pulmonary Tuberculosis. J. O. Parramore, Crown Point.—p. 602.  
Tuberculous Pneumonia. J. W. Strayer, Lafayette.—p. 605.  
Surgical Treatment of Pulmonary Tuberculosis. J. H. Stygal, Indianapolis.—p. 609.  
Tuberculosis: Where Do We Go from Here? G. C. Johnson, Evansville.—p. 612.  
The Future Outlook in Tuberculosis. M. H. Draper, Fort Wayne.—p. 614.  
Eventration of the Diaphragm Following Empyema: Case Report. G. A. Dickinson, Petersburg.—p. 615.  
Complete Rupture of the Uterus. G. W. Gustafson and W. E. Crump, Indianapolis.—p. 616.

# Johns Hopkins Hospital Bulletin, Baltimore

63: 283-348 (Nov.) 1938

- Effect of Preventing Development of Hypersensitivity in Experimental Tuberculosis. R. H. Follis Jr., Baltimore.—p. 283.  
Spirocheticidal Action of Bismuth Compounds on Pathogenic Spirocheta Pallida in Vitro. H. Eagle, Baltimore.—p. 305.  
\*Absorption and Excretion of Certain Sulfanilamide Derivatives. E. K. Marshall Jr., W. C. Cutting and W. L. Cover, Baltimore.—p. 318.  
Absorption and Excretion of Sulfanilamide in Mouse and Rat. E. K. Marshall Jr. and W. C. Cutting, Baltimore.—p. 328.  
\*Passage of Sulfanilamide Through the Human Placenta. H. Speert, with technical assistance of Dorothea Babbitt, Baltimore.—p. 337.  
Delayed Toxic Reaction to Sulfanilamide: Case Report. L. Danziger, Baltimore.—p. 340.

**Absorption and Excretion of Sulfanilamide.**—Marshall and his associates compared the absorption and excretion in dogs of moderately soluble sulfanilamide, easily soluble mono-ethanol sulfanilamide and slightly soluble disulfanilamide. They found that ethanol sulfanilamide is absorbed and also excreted very rapidly, while disulfanilamide is absorbed slowly and excreted rapidly in comparison with sulfanilamide. Little increased absorption occurs with a large dose of the easily insoluble compound as compared with a small one. Sulfanilamide when given in solution by mouth is absorbed much more quickly than when



given in solid form. Absorption is slight from the stomach but rapid from the intestine. Sulfanilamide derivatives do not all pass into the spinal fluid as readily as does sulfanilamide.

**Passage of Sulfanilamide Through Human Placenta.**—Speert studied the transmission of sulfanilamide through the human placenta. His studies confirm those of Lee, Anderson and Chen that the drug passes readily from mother to fetus. The sulfanilamide concentration of the fetal blood rapidly approaches that of the mother, equilibrium being reached within approximately five hours. This was true for both the free and the acetylated forms of the drug, a finding at variance with the results of the foregoing authors. The concentration of sulfanilamide in the amniotic fluid indicates a correspondingly free passage of the drug. Clinically, infants show no ill effects from the drug either at birth or during the neonatal period. The data presented represent the placental transmission of sulfanilamide in the human being only at term. It is entirely possible that in earlier stages of pregnancy great differences from the present observations may occur.

### Journal of Bacteriology, Baltimore

36: 337-454 (Oct.) 1938. Partial Index

- Apparent Oxidation-Reduction Potentials of Bright Platinum Electrodes in Synthetic Medium Cultures of Bacteria. W. E. Ward, Chicago.—p. 337.  
Heat Sterilized Reducing Sugars and Their Effects on Thermal Resistance of Bacteria. J. G. Baumgartner, London, England.—p. 369.  
Micro-Organism Decomposing Group Specific Substances. M. W. Chase, New York.—p. 383.  
Relationships of Coliform Organisms. C. A. Stuart, A. M. Griffin and Muriel E. Baker, Providence, R. I.—p. 391.  
Coliform Organisms in Certified Milk. C. A. Stuart, K. M. Wheeler and A. M. Griffin, Providence, R. I.—p. 411.  
Comparative Studies on Purification of Tetanus and Diphtheria Toxins. M. D. Eaton and A. Gronau, St. Louis.—p. 423.  
Oxidations Produced by Hemolytic Streptococci. E. S. G. Barron and H. R. Jacobs, Chicago.—p. 433.

### Journal of Experimental Medicine, New York

68: 641-788 (Nov.) 1938

- Reactions of Normal and Tuberculous Animals to Tuberculo-protein and Tuberculophosphatide. K. C. Smithburn and Florence R. Sabin, New York.—p. 641.  
\*Tubercular Allergy Without Infection. Florence R. Sabin and A. L. Joyner, New York.—p. 659.  
\*Studies on Eastern Equine Encephalomyelitis: I. Histopathology of Nervous System in Guinea Pig. L. S. King, Princeton, N. J.—p. 677.  
Production by New Method of Renal Insufficiency and Hypertension in Rabbit. D. R. Drury, Los Angeles.—p. 693.  
Immunologic Reactions with Virus Causing Papillomas in Rabbits: I. Demonstration of Complement Fixation Reaction: Relation of Virus-Neutralizing and Complement-Binding Antibodies. J. G. Kidd, New York.—p. 703.  
Id.: II. Properties of Complement-Binding Antigen Present in Extracts of Growths: Its Relation to Virus. J. G. Kidd, New York.—p. 725.  
Id.: III. Antigenicity and Pathogenicity of Extracts of Growths of Wild and Domestic Species: General Discussion. J. G. Kidd, New York.—p. 737.  
Intraperitoneal and Intracerebral Routes in Serum Protection Tests with Virus of Equine Encephalomyelitis: II. Mechanism Underlying Difference in Protective Power by Two Routes. P. K. Olitsky and C. G. Harford, New York.—p. 761.  
Id.: III. Comparison of Antiviral Serum Constituents from Guinea Pigs Immunized with Active or Formalized Inactive Virus. P. K. Olitsky and C. G. Harford, New York.—p. 779.

**Tuberculous Allergy Without Infection.**—On the basis of their studies Sabin and Joyner conclude that guinea pigs can be rendered hypersensitive to tuberculo-protein by small, repeated, intradermal injections of active tuberculo-protein. The addition of tuberculophosphatide to the protein speeds up the process of sensitization and enhances it so that the reactions become indurated and necrotic, closely simulating those of the disease. Active tuberculo-proteins induce a new formation of monocytes and some epithelioid cells. The addition of phosphatide to the protein brings about a massive formation of epithelioid cells. The increase in the speed and intensity of the sensitization may be correlated with the increased cellular reaction to the mixed injections. The intradermal route is the best for these sensitizations, probably because it provides the greatest dose per cell of the sensitizing agent. The degree of sensitization artificially obtainable by the synergistic action of tuberculophosphatide and tuberculo-protein is quite comparable to the degree of sen-

sitization naturally occurring in tuberculous animals; moreover, this degree of sensitization may be induced with amounts of the materials from the bacilli which could conceivably be present in the tissues of an infected host.

**Eastern Equine Encephalomyelitis.**—King studied the neuropathologic features of equine encephalomyelitis in the guinea pig. The histogenesis of the disease process is described. After peripheral inoculation the earliest detectable pathologic change is the accumulation of leukocytes within the lumen of the blood vessels and the proliferation of the vascular adventitia. This precedes the appearance of any significant perivascular cuffing and may or may not be accompanied by a few polymorphonuclear leukocytes. The typical lesion is a fairly well circumscribed focus of polymorphonuclear leukocytes accompanying the foregoing vascular changes. The leukocytes may be numerous or sparse and may or may not be accompanied by neuron destruction. The neocortices and olfactory cortices are the principal sites of predilection. A distinction between inflammatory and degenerative lesions depends on the relationship between the neuron destruction and the exudative changes. After intracerebral inoculation the inflammatory changes are much less marked than after peripheral inoculation. This is due to a different type of pathologic process. Following intracerebral inoculation there is primary destruction of neurons, involving especially the hippocampus and also large areas of the neocortex. This change, similar to ischemic necrosis, is regarded in part as a nonspecific reaction of especially vulnerable tissue.

### Military Surgeon, Washington, D. C.

83: 275-400 (Oct.) 1938

- Indications for and Value of Various Types of Sympathectomy. A. W. Adson.—p. 275.  
Observations at the Mayo Clinic. C. L. Leedham.—p. 294.  
Malaria in the Panama Canal Department, United States Army: I. Incidence of Primary Cases in 1936 and 1937. G. R. Callender and C. J. Gentzkow.—p. 299.  
Low Back Pain. F. A. Jostes.—p. 316.  
Chronic, Intractable Ulcerative Colitis. F. R. Sedgley.—p. 326.  
Importance of Medicodental Cooperation. O. A. Oliver.—p. 329.  
History of the 102d Medical Regiment New York National Guard. L. A. Salisbury.—p. 339.  
Medical Field Service School, U. S. Marine Barracks, Quantico, Va. H. E. Gillespie.—p. 343.  
Statistical Study of 1,781 Appendectomies in CCC Personnel of the Fourth Corps Area from 1933 to 1936, with Especial Reference to Comparative Mortality Rates. F. F. Rudder.—p. 345.

### New England Journal of Medicine, Boston

219: 685-730 (Nov. 3) 1938

- Relation of Dermatology to General Medicine. G. A. Dix, Worcester, Mass.—p. 685.  
Lupus Erythematosus Discoides: Its Present Status with Regard to Etiology and Treatment. M. M. Tolman, Boston.—p. 688.  
Are Patch Tests of Real Value in Dermatology? J. G. Downing, Boston.—p. 698.  
Use of Scratch Test in Dermatology, with Special Reference to Atopic Dermatitis. J. Goodman, Boston.—p. 705.  
Syphilitic Scars of the Spirit. A. W. Cheever, Boston.—p. 709.

### New Orleans Medical and Surgical Journal

91: 211-270 (Nov.) 1938

- Possible Role of Intestinal Toxemia in Liver Damage. A. Eustis, New Orleans.—p. 211.  
Traumatic Stricture of Cervix. H. E. Miller and C. G. Collins, New Orleans.—p. 216.  
Ruptured Pyosalpinx. N. J. Tessitore and J. S. Potekin, New Orleans.—p. 222.  
Hyperthyroidism. R. B. Wallace, Alexandria.—p. 226.  
Thrombocytopenic Purpura: Three Case Reports. J. G. Snelling, Monroe, La.—p. 231.  
Determination of Vitamin C Deficiency. Grace A. Goldsmith, New Orleans, and G. F. Ellinger, Mount Vernon, Wash.—p. 237.  
Ruptured Intervertebral Disk: Cause of Sciatic Pain. D. H. Echols, New Orleans.—p. 243.  
\*Pregnant Woman with Lobar Pneumonia, Type VIII, Cured by Specific Serum. J. H. Musser and M. J. Boggs, New Orleans.—p. 246.

**Recovery from Lobar Pneumonia in Pregnancy.**—Musser and Boggs report the case of a woman seven months pregnant who recovered from type VIII pneumonia after specific serum therapy was given on the second day of illness. The patient was tested for sensitivity by the conjunctival method and the reaction was negative. She was then given 10,000 units of type VIII antipneumococcus serum prepared from rabbits' serum, two hours later she was given 40,000 units intravenously,

four hours later 40,000 units, and this was repeated in another four hours. The day after the serum was administered the patient's temperature was normal, her extreme cyanosis and dyspnea, which required oxygen, had disappeared and five days later she was discharged from the hospital entirely well.

### Ohio State Medical Journal, Columbus

34: 1197-1308 (Nov.) 1938

- Passive Prophylaxis Against Acute Infections in Childhood. J. A. Toomey, Cleveland.—p. 1213.  
Chronic Gastritis: Present Day Status: Part I. L. Schiff and S. Goodman, Cincinnati.—p. 1220.  
Surgical Treatment of Diverticulitis. T. E. Jones, Cleveland.—p. 1225.  
\*Surgical Treatment of Epilepsy. J. P. Evans, Cincinnati.—p. 1229.  
Membranes. F. S. Mowry, Cleveland.—p. 1232.  
Technic for Mastoideotomies Under Local Anesthesia. M. E. Scott, Massillon.—p. 1235.  
Treatment of Prenatal Syphilis. E. W. Netherton, Cleveland.—p. 1237.  
Perirectal Abscesses. W. W. Green, Toledo.—p. 1245.  
Gonorrheal Infection in Children Treated with Sulfanilamide: Report of Fifty Cases. J. E. Hoberg, Columbus, and L. E. Reck, Adrian, Mich.—p. 1249.  
Carbon Monoxide Poisoning. H. A. Martin, Toledo.—p. 1251.

**Surgical Treatment of Epilepsy.**—Evans states that the first requirement of selecting cases of epilepsy for surgical intervention is that the epilepsy be due to focal lesions in the brain. It might then appear that any generalized seizure would be excluded from consideration at the outset. This, however, is not always so, for it is conceivable that a seizure firing, for example, from one of the frontal poles, might work up its abnormal cerebral rhythm in a silent area of the brain and that the seizure would then spread rapidly, firing off the entire body musculature at one time. It is the usual rule, however, that cases of generalized seizures less often prove susceptible to surgical intervention. It is essential to analyze carefully both the subjective and the objective course of events in the patient's seizure and thus sort out by detailed analysis signs which indicate the initial area of abnormal discharge. Another criterion for the selection of cases suitable for surgical intervention is the pneumo-encephalographic evidence of focal damage. A third criterion is the finding at the site of suspected pathologic change variations of electrical potential characteristic of epileptic discharge. Use of this method depends on further elaboration of the methods of electro-encephalography. However, before radical excision of the suspected area is undertaken, a fourth criterion should be met—the production of a characteristic seizure by carefully controlled electrical stimulation of the exposed cortex. Finally, any patient should have, before operation is seriously considered, a thorough trial of phenobarbital or other sedative therapy, partly to avoid unnecessary operation, partly to prove that any postoperative sedation employed is not the cause of postoperative improvement rather than the operation itself. The aim of operative intervention is to excise the damaged area of the brain, leaving a lesser degree of damage than was caused by the original injury. This involves an understanding of the anatomic arrangement of the blood vessels and of the physiology of collateral circulation. The author concludes that the results of radical excision of cerebral cicatrix are, in his opinion, such as to justify further intelligent and critical pursuit of the problem.

### Physiological Reviews, Baltimore

18: 481-596 (Oct.) 1938

- Formation of Egg of Domestic Fowl. R. M. Conrad and H. M. Scott.—p. 481.  
Application of Law of Chemical Equilibrium (Law of Mass Action) to Biologic Problems. F. C. McLean, Chicago.—p. 495.  
Plant Growth Hormones. K. V. Thimann, Cambridge, Mass., and J. Bonner, Pasadena, Calif.—p. 524.  
Physiologic Effects of Small Amounts of Lead: Evaluation of Lead Hazard of the Average Individual. A. S. Minot, Nashville, Tenn.—p. 554.  
Factors Concerned in Duration of Pregnancy. F. F. Snyder, Baltimore.—p. 578.

### Public Health Reports, Washington, D. C.

53: 1907-1960 (Oct. 28) 1938

- Disabling Sickness Among Male Industrial Employees During the Second Quarter and the First Half of 1938. W. M. Gafafer and Elizabeth S. Frasier.—p. 1910.  
Studies of Sewage Purification: VIII. Observations on Effect of Variations in Initial Numbers of Bacteria and of Dispersion of Sludge Flocs on Course of Oxidation of Organic Material by Bacteria in Pure Culture. C. T. Butterfield and Elsie Wattie.—p. 1912.

### Radiology, Syracuse, N. Y.

31: 391-520 (Oct.) 1938. Partial Index

- Roentgen Kymography as Diagnostic Aid. P. Stumpf, Munich, Germany.—p. 391.  
Roentgenologic Diagnosis of Tumors Involving the Sacrum. J. D. Camp and C. A. Good Jr., Rochester, Minn.—p. 398.  
Roentgenographic Demonstration of Pulmonary Veins. B. S. Epstein, Brooklyn.—p. 418.  
Emphysematous Cholecystitis and Pericholecystitis. E. A. Schmidt, Denver.—p. 423.  
\*Variations in Position of Normal Coccyx. L. J. Friedman and C. Stein, New York.—p. 438.  
Osseous Growth and Development. E. C. Vogt and Vernet S. Vickers, Boston.—p. 441.  
Coarctation of the Aorta: Three Cases with Necropsy Findings in One. T. B. Weinberg and C. Gartenlaub, New York.—p. 445.  
Effect of Radiation Applied Directly to the Brain and Spinal Cord: I. Experimental Investigations on Macacus Rhesus Monkeys. L. M. Davidoff, C. G. Dyke, C. A. Elberg and I. M. Tarlov, New York.—p. 451.  
Concerning Diagnosis of Lesions in Lower Spinal Canal. J. C. Bell and R. G. Spurling, Louisville, Ky.—p. 473.

**Variations in Position of Normal Coccyx.**—Friedman and Stein observed the position of the coccyx in 100 adults, chosen at random, who were free of any symptoms referable to the spine and who had no history of trauma to the sacrum or coccyx. Roentgenograms were taken in the anteroposterior and lateral positions. Angulations (from 5 to 65 degrees) at the sacrococcygeal and first coccygeal articulations are to be found in the normal spine. The variation may occur either in the transverse or sagittal plane and, more rarely in both.

### Rocky Mountain Medical Journal, Denver

35: 833-936 (Nov.) 1938

- Roentgen Diagnosis of Acute Abdominal Conditions. L. G. Rigler, Minneapolis.—p. 850.  
Surgical Complications Resulting from Presence of Heterotopic Tissue in Meckel's Diverticulum. W. C. Black and G. B. Packard, Denver.—p. 859.  
Acute Lymphocytic Meningitis. P. A. Draper, Colorado Springs, Colo.—p. 863.  
Mrs. Brown Has Boy in Spite of Lots of Things. C. B. Ingraham, Denver.—p. 867.

### South Carolina Medical Assn. Journal, Greenville

34: 279-302 (Nov.) 1938

- Serum Therapy in Lobar Pneumonia. W. H. Kelley, Charleston.—p. 279.  
Difficulties in Abdominal Diagnosis in Children—Illustrative Cases. D. Jennings, Bennettsville.—p. 282.  
Retropharyngeal Abscess. C. W. Evatt, Charleston.—p. 287.

### Surgery, St. Louis

4: 649-808 (Nov.) 1938

- Treatment of Paralytic Bladder in Cases of Spinal Cord Injury. F. Hinman, San Francisco.—p. 649.  
Tumors of Kidney Which Invade Inferior Vena Cava: Report of Seven Cases. J. H. Tillisch, H. C. Habein and J. C. Henthorne, Rochester, Minn.—p. 663.  
Role of Urea-Splitting Organisms in Formation of Certain Types of Stones in Urinary Tract. E. Burns, New Orleans.—p. 673.  
\*Use of Vitamin B<sub>1</sub> in Preoperative Preparation of Hyperthyroid Patient. W. D. Frazier and I. S. Ravdin, Philadelphia.—p. 680.  
Nonoperative Treatment of Perforated Gastric Ulcer with Generalized Peritonitis by Continuous Gastric Siphonage. P. Nagle, Oklahoma City.—p. 687.  
Acidity of Gastric Contents After Excision of Antral Mucosa. E. B. Lewis, Rochester, Minn.—p. 692.  
Wandering Spleen with Torsion of the Pedicle: A Patient Treated by Splenectomy with Alarming Events During Convalescence. P. E. Truesdale and D. Freedman, Fall River, Mass.—p. 700.  
Endometrial Tumors in Postcancerous Abdominal Laparotomy Scars. P. A. Kaufman and A. O. Wilensky, New York.—p. 708.  
Etiology of Vasomotor and Nutritional Changes Following Peripheral Nerve Section. L. N. Atlas, Cleveland.—p. 718.  
New Modification of Subarachnoid Alcohol Injection for Bilateral Blocking of Lower Sacral Nerves in Intractable Pain of Pelvic Viscera. J. C. White, Boston.—p. 722.  
Acute Aerobic (Nonputrid) Abscess of Lung. H. Neuhoef and A. S. W. Touroff, New York.—p. 728.  
\*Incidence of Air-Borne Bacteria in the Major Surgery of Multnomah County Hospital. O. M. Nisbet and J. W. Brooke, Portland, Ore.—p. 755.  
Osteopetrosis: Report of Three Cases. K. M. Lippert, Richmond, Va.—p. 762.  
Rupture of Esophagus in a Child Two Years of Age, with Recovery. C. D. Benson and G. C. Penberthy, Detroit.—p. 777.

**Preoperative Vitamin B<sub>1</sub> and Thyroidectomy.**—The evidence that a vitamin B complex or B<sub>1</sub> deficiency may play a part in the production of certain of the gastrointestinal disturbances, especially the anorexia often exhibited by the hyper-

thyroid patient, is discussed by Frazier and Ravdin. Several years ago they began the use of a vitamin B complex extract in patients suffering from hyperthyroidism. The patients were given large amounts of the extract with no other therapy during the period of observation. Although the basal metabolic rate was not reduced any more than in a control group, the general condition of the patients given the vitamin was better than the control group. The beneficial effects of the vitamin were compared with that of twenty-eight patients similarly treated in every respect except that no vitamin B was administered. The routine preoperative treatment was complete bed rest except for two hours daily, high caloric, high carbohydrate diet consisting of from 3,000 to 4,000 calories daily, from 5 to 10 minims (0.3 to 0.6 cc.) of saturated solution of potassium iodide three times a day, 0.65 Gm. of sodium bromide three times a day and 1½ grains (0.1 Gm.) of phenobarbital nightly. The fifty vitamin treated patients received in addition to the foregoing regimen 10 mg. of crystalline vitamin B<sub>1</sub> hypodermically every other day and 10 Gm. of brewers' yeast daily by mouth. Improvement in the vitamin treated patients, over the control group, occurred to the degree that the pulse rate was reduced during the period of preparation, patients gained weight and their appetite was increased and the length of time required for adequate preoperative preparation was shortened. These results are in agreement with the known effect of vitamin B<sub>1</sub> on the cardiovascular and gastrointestinal systems, if some degree of vitamin B deficiency exists. The two series of patients showed no significant differences in the lowering of the basal metabolic rate before operation or in the severity of the postoperative reaction. When improvement was noted in the vitamin treated series it was most marked in the more toxic group.

**Air-Borne Bacteria.**—Nisbet and Brooke found that the number of air-borne bacteria in the major surgery rooms of Multnomah County Hospital is roughly proportional to the number of persons present and to the activity on the floor proper of the surgery. The greatest proportionate rise in incidence is manifested by the streptococci and Staphylococcus albus. The organisms showing this rise are acknowledged to be common inhabitants of the nasopharynx. The estimated number of bacteria falling per hour on a sterile operating field compares unfavorably with similar figures obtained in other hospitals. The assumption that this increase is due in part to the agitation of air currents caused by the passage of the operating room assistants does not appear to be unwarranted. It is possible that some bacteria are carried into the surgery by the footwear.

### Tennessee State Medical Assn. Journal, Nashville 31: 381-424 (Oct.) 1938

- \*Sterilization of the Female by Cauterization of Uterine Cornu. C. G. Bowers and Margaretta Keller Bowers, Lyles.—p. 381.  
Comparative Aspects in Treatment of Syphilis. E. R. Hall, Memphis.—p. 388.  
The Changing Pediatric Picture. E. Rosamond, Memphis.—p. 393.

**Sterilization of the Female.**—The Bowerses present a method for the sterilization of women for which hospitalization is not necessary. The procedure can be carried out in the office as it is only slightly more disturbing than cervical cauterization. After determining the necessity for sterilization, the patient is requested to be at the office a week or ten days after her regular menstrual period. She is instructed to take a copious douche of warm soda water an hour before her appointment. Following pelvic palpation she is left in the lithotomy position and a Sims speculum is introduced. The vagina and vaginal wall are thoroughly swabbed with a suitable antiseptic. The plug of mucus occluding the os is removed and the cervical canal is cleaned. A lip of the cervix is grasped with a tenaculum, and a catheter to which is attached a syringe with 10 cc. of radiopaque oil is inserted until its tip passes the internal os and the rubber olive fits snugly into the canal. The oil is injected slowly. The injection is discontinued, but the catheter is retained in position to prevent outflow of oil. A roentgenogram is taken and immediately developed, outlining the cavity of the tubes and uterus. The electrode employed is about 9 inches long and one-fifth inch in diameter; the distal end is semiflexible and is tipped with a small conical coil of platinum wire. Proxi-

mally there are two leads for electrical connections. The cauterizing coil at the tip is of platinum wire. To bring the cautery to a "cherry red" in air it was found that  $8 \pm 0.1$  amperes was required, corresponding to a consumption of 0.96 watt. The cautery electrode is then introduced, following the route previously outlined by the sound. Its active tip is snugly fitted into the uterine horn and by touch on its shank it is determined to be in contact with the mucosa on all sides. The current is then turned on for about forty-five seconds; meanwhile the active tip is given a slow rotary motion of a single revolution. This movement of the cautery tip prevents too deep a burn in one spot in the cornu and it causes the cauterization to be distributed about the entire funnel surface of the cornu, causing destruction of all the mucosa in this area and giving assurance against fistulous formation. It is important that the zone of coagulation extend into the muscular wall of the uterus, as it is here that the contracture is produced. The opposite side is similarly cauterized and a gauze sponge is left in the vagina to absorb the oily and sanguineous exudate, which the patient is instructed to remove when she returns home. Within a few days following the treatment there will be a serosanguineous discharge for a week or so which may necessitate a daily cleansing douche. Six weeks after the cauterization the patency of the tubes is checked either by air insufflation or roentgenologically. If the tube is closed, the cornu will be seen to be dome shaped and no oil will enter the tube. Contraindications for carrying out the procedure include any active infection of the genito-urinary system or any chronic infection of the tubes or uterus. Patients with malignant growths, fibroids, polyps and endometritis should not be treated with the cautery electrode. Of a series of twelve patients, six were cauterized once, five were cauterized twice and one was cauterized three times before closure was complete.

### Virginia Medical Monthly, Richmond

65: 651-722 (Nov.) 1938

- A Few Leaves from the Diary of That Fast Disappearing Representative of the Genus Homo, the Country Doctor. G. F. Simpson, Purcellville.—p. 651.  
Pioneering in Health—1908 to 1910. R. K. Flannagan, Richmond.—p. 655.  
Painless Childbirth Made Safe with Paraldehyde. S. M. Dodek, Washington, D. C.—p. 661.  
Current Methods of Treating Mental Cases in Virginia. H. C. Henry, Richmond.—p. 664.  
Important Points to Be Remembered About Crossed Eyes: Lantern Demonstrations. J. A. Pilcher Jr., Roanoke.—p. 667.  
Syphilis in Childhood. Louise Fry Galvin, Richmond.—p. 670.  
The Physician's Role in Adoption. Lois Benedict, Roanoke, and B. B. Jones, Richmond.—p. 674.  
\*Eleven Cases of Toxemia of Pregnancy Treated with Progesterone. W. McMann, Danville.—p. 676.  
Use of Insulin in Certain Psychiatric Disorders. R. M. Crowley, Rockville, Md.—p. 678.  
Hemorrhage from Upper Gastrointestinal Tract: Its Medical Management: A Review. J. F. Waddill, Norfolk.—p. 682.  
The Management of the Heart in Pregnancy. E. Podolsky, Brooklyn.—p. 686.

**Toxemia of Pregnancy Treated with Progesterone.**—McMann used a preparation of corpus luteum hormone in the treatment of eleven cases of toxemia of pregnancy. No other treatment was given. Labor was induced when the prognosis seemed precarious. The final results were disappointing. There were three absolute failures, two were questionable and six patients seemed to respond to treatment. The response, however, was greater than when the dehydration principles of Arnold and Fay, coupled with rest and strict attention to diet, are used.

### West Virginia Medical Journal, Charleston

34: 485-532 (Nov.) 1938

- Recent Advances in Treatment of Pneumonia. D. A. MacGregor, Wheeling.—p. 485.  
Statistics on Lobar Pneumonia, from a West Virginia Hospital. W. L. Cooke, Charleston.—p. 494.  
The Art of Diagnosis. J. C. Gittings, Philadelphia.—p. 497.  
Syphilis in Mining Communities. W. P. Bittering, Summerlee.—p. 506.  
Pulmonary Suppuration. L. H. Clerf, Philadelphia.—p. 513.  
Local Anesthetic Crises in Rhinology. Sobieska S. Hall and H. V. Thomas, Clarksburg.—p. 516.  
Rat-Bite Fever: Case Report. J. E. Fisher, New Cumberland.—p. 521.

## FOREIGN

An asterisk (\*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

**British Journal of Physical Medicine, London**

1: 331-366 (Oct.) 1938

- Rheumatism and Electrotherapy. W. Beaumont.—p. 332.  
Chronic Arthritis in Women. C. A. Robinson and V. C. Robinson.—p. 340.  
Occupational Therapy in Treatment of Arthritis. W. S. C. Copeman.—p. 350.  
Diet in Rheumatic Diseases. J. A. Nixon.—p. 353.

**British Journal of Surgery, Bristol**

26: 217-456 (Oct.) 1938. Partial Index

- Abdominal Injuries and Their Recipients. G. Gordon-Taylor.—p. 217.  
Transphenoidal Decompression for Pituitary Adenoma. G. Phillips.—p. 242.  
Investigation into Condition of Bladder Mucosa in Relation to Stone Formation. J. Gray.—p. 259.  
Saccular Aneurysms of Internal Carotid Artery in Cavernous Sinus. G. Jefferson.—p. 267.  
Carcinoid Tumors of Appendix. T. Moore.—p. 303.  
\*Endothelioma of Pleura: Two Cases. N. R. Barrett and J. St. C. Elkington.—p. 314.  
Operation for Recurrent Dislocation (Subluxation) of Sternoclavicular Joint. A. S. B. Bankart.—p. 320.  
Nerve Supply of Gastro-Esophageal Junction. G. A. G. Mitchell.—p. 333.  
Extradural Hemorrhage. K. G. McKenzie.—p. 346.  
Spinal Epidural Suppuration, with Special Reference to Osteomyelitis of Vertebrae. F. A. R. Stammers.—p. 366.  
Recurrent Dislocation of Shoulder: A Plea for Simple Operation. E. W. H. Groves.—p. 375.  
\*Granulomatous Ulcers Resembling Tuberculous Ulcers of the Stomach. M. G. Kini and M. Narasimha Rao.—p. 379.  
Simultaneous Perforation of Multiple Peptic Ulcers. W. E. Austin.—p. 387.  
Surgical Treatment of Obstructive Jaundice in Pancreatic Disease. J. Fraser.—p. 393.  
Behavior of Blood Volume in Intestinal Obstruction and Strangulation. I. Aird.—p. 418.  
Sarcoma of Intestine in Children. A. Simpson-Smith.—p. 429.

**Endothelioma of Pleura.**—There is no general agreement that endothelioma of the pleura exists as a pathologic or a clinical entity. Barrett and Elkington do not enter into this controversy but rather point out and explain some physical signs which they found in two cases of diffuse new growth of the pleura. In both cases a careful postmortem examination was made. In neither was a primary tumor demonstrable in the bronchial tree nor was there any evidence of lymphatic invasion in spite of the fact that the growths were extensive. In the second case malignant cells were found in the sputum before death, and these were diagnosed as from an endothelioma. At the postmortem examination of this case it was obvious that the malignant tissue was invading the bronchi from without, and paraffin sections showed the mucosa intact in places in which collections of malignant cells had penetrated between the cartilaginous rings and extended along the submucosa. The fact that malignant cells were ultimately demonstrable in the sputum is not necessarily an argument in favor of the suggestion that this was a primary bronchial growth. From the clinical point of view, both these tumors gave physical signs which were difficult to interpret in the early stages. In each case the respiratory signs pointed to a marked, progressive and diffuse thickening of the pleura, with little evidence of involvement of the lung itself. The nervous signs were strikingly similar. They consisted of wasting and complete paralysis of certain of the intercostal muscles on one side and also of the upper segment of the abdominal recti and oblique muscles. In each case the diaphragm on that side was immobile.

**Granulomatous and Tuberculous Gastric Ulcers.**—Kini and Narasimha Rao state that when extensive shallow ulcers with undermined edges occur in the pyloric region it becomes difficult to differentiate them from malignant disease of the pyloric antrum. After gastrectomy one of the three ulcers in their series, which appeared to the naked eye to be typically tuberculous, failed to show on microscopic examination any evidence of tuberculosis (case 3). Case 1 was diagnosed as a case of malignant disease and a gastrectomy was performed. It was only after gastrectomy that the ulcer was found to be granuloma-

tous, resembling a tuberculous ulcer, which on microscopic examination it was suspected to be. In case 2 no gastrectomy could be performed, as the general condition of the patient was poor. While gastro-enterostomy was being performed, a good view of the ulcer could be obtained through the stoma. It resembled the ulcer in case 1. The gland removed for biopsy was suspected to be tuberculous on microscopic examination. Case 3 resembled the first in all its aspects, but on histologic examination there was no evidence of tuberculosis in the sections examined. A gastrectomy was performed.

**British Journal of Tuberculosis, London**

32: 205-260 (Oct.) 1938

- What Can Be Done to Prevent the Tuberculous Patient from Relapsing? G. C. Williams.—p. 208.  
Id. H. G. Trayer.—p. 211.  
The Prevention of Relapse in Cases of Pulmonary Tuberculosis. F. H. Young.—p. 216.  
The Prevention of Relapse in the Tuberculous Patient: An After-Care Problem. K. N. Irvine.—p. 221.  
What Can Be Done to Prevent the Tuberculous Patient from Relapsing? A. M. Cooke.—p. 225.  
Pleural Perforation in Pulmonary Tuberculosis: Character of Pleural Exudate: Diagnosis of Perforation by Gas Analysis. H. Harpöth and U. Gad.—p. 228.  
Tomography. H. Roche.—p. 236.

**Journal of Laryngology and Otology, London**

53: 625-684 (Oct.) 1938

- \*Observations on the Pathology of Ménière's Syndrome. C. E. Hallpike and H. Cairns.—p. 625.  
Osteoclastoma of Frontal Bone in Hyperparathyroidism. R. P. Mathers and D. F. Cappel.—p. 656.

**Pathology of Ménière's Syndrome.**—Hallpike and Cairns describe the microscopic changes in the temporal bones of two patients with Ménière's syndrome. In each of these the affected temporal bone showed a gross distention of the endolymphatic system together with degenerative changes in the sensory elements. A possible explanation of this distention is suggested by the absence in both patients of the normal area of perisaccular connective tissue around the saccus endolymphaticus. A possible mechanism is further suggested whereby the microscopic changes may be correlated with the clinical features of the disease.

**Journal of Physiology, London**

94: 1-186 (Oct. 14) 1938. Partial Index

- Factors in Sexual-Skin Edema. Olive E. Aykroyd and S. Zuckerman.—p. 13.  
Effect of High Doses of Androgenic Substances on Weights of Testes, Accessory Reproductive Organs and Endocrine Glands of Young Male Guinea Pigs. A. C. Bottomley and S. J. Folley.—p. 26.  
Influence of Glycotropic (Anti-Insulin) Factor of Anterior Hypophysis on Insulin Sensitivity of Hypophysectomized Rabbit. W. H. Newton and F. G. Young.—p. 40.  
Undernutrition and Liver Fat. C. H. Best and Jessie H. Ridout.—p. 47.  
Electrical Activity of Cerebellum and Its Functional Significance. R. S. Dow.—p. 67.  
Action of Ephedrine. J. H. Gaddum and H. Kwiatkowski.—p. 87.  
\*Chloride Content of Blood Serum and Aqueous Humor: Its Relation to Glaucoma and to Formation of Intra-Ocular Fluid. T. H. Hodgson.—p. 118.  
Water Balance and Blood Changes Following Posterior Pituitary Extract Administration. E. C. Dodds, S. H. Liu and R. L. Noble.—p. 124.  
Action of Nicotine on Spinal Cord. A. Schweitzer and S. Wright.—p. 136.  
\*Absorption and Excretion of Iron Following Oral and Intravenous Administration. R. A. McCance and E. M. Widdowson.—p. 148.  
Liberation of Acetylcholine by Perfused Superior Cervical Ganglion. F. C. MacIntosh.—p. 155.  
Functional Impairment of Anterior Pituitary Gland Produced by Synthetic Estrogenic Substance 4: 4' Dihydroxy- $\alpha$ :  $\beta$ -Diethylstilbene. R. L. Noble.—p. 177.

**Chloride Content of Blood Serum and Aqueous Humor.**—Hodgson determined the chloride content of the aqueous humor and blood serum of man and dogs by the ultramicro silver iodate method. The values for a group of nonglaucomatous human beings averaged, in millimols per liter, aqueous 124.3, serum 105.1. There was no significant difference in the values obtained in cases of primary chronic glaucoma with high intra-ocular tension in which the average values were 126.3 for aqueous and 106.5 for serum. Normal unanesthetized dogs gave average values of 127.6 and 109.1, respectively. The high values

obtained for aqueous chloride show that there is no Donnan equilibrium for this ion between the blood and the aqueous humor, so that the latter cannot be regarded as a dialysate.

**Intestinal Absorption and Excretion of Iron.**—McCance and Widdowson discuss experiments planned to determine whether or not the intestine of a normal human being can excrete iron and by so doing regulate the amount of iron in the body. The investigation consisted of three stages: diets containing daily from 5.9 to 8.6 mg. of iron, from 12 to 16 mg. of iron and from 7.6 to 11.7 mg. in addition to 7 mg. of iron intravenously. Within the limits of experimental error none of the injected iron was excreted into the gastrointestinal tract. About 1.4 per cent of it was excreted in the urine, but it is believed that this is of no practical significance in iron metabolism. The results are considered to confirm the theory that the intestine has no power of regulating by excretion the amount of iron in the body. The three normal women were not in positive iron balance in their intermenstrual periods. It would be interesting to know at what time during the menstrual cycle these women absorbed the iron necessary to make good their loss.

### J. Royal Inst. Public Health and Hygiene, London

1: 695-758 (Sept.) 1938

- \*Influences Which Undermine the Health of Women. A. Bourne.—p. 705.  
The General Practitioner and Tuberculosis. K. McFadyen.—p. 712.  
Some Experiences of Slum Clearance Procedure in Manchester. A. M. M. Grierson.—p. 724.  
Postural and Occupational Factors in Rheumatic Pain. A. Wesson.—p. 733.  
Essentials of Nutrition in Infants and Toddlers. B. E. Myers.—p. 736.

1: 759-822 (Oct.) 1938

- Changing Views as to Spread of Infection. C. O. Stallybrass.—p. 769.  
Id. H. G. Smith.—p. 781.  
Tuberculosis in Relation to the Pneumoconioses. J. V. Sparks.—p. 790.  
Incidence and Significance of "Growing Pains" in Children and Adolescents. J. C. Hawksley.—p. 798.  
Heart Disease and Pregnancy. J. W. Brown.—p. 806.  
Respiratory Diseases in Children. W. Pearson.—p. 811.

**Health of Women.**—Bourne states that a great volume of the minor but chronic ill health of women is due not so much to the major difficulties or injuries of reproduction or even to the peculiar susceptibility of the pelvic organs to disease but to the wearing influence of a mass of minor worries incidental to their domestic and family life. Two main influences may affect the spinster's health. The first, a deep disappointment of the maternal instinct coupled with an underlying fear of economic insecurity, is liable to express itself physically in neurosis. The author believes that the majority of women who have not found a mate, and who have no absorbing work or object on which to exert their desire for service, do suffer in a way that will ultimately express itself physically. In the second influence it is probable that the exclusion from activity of the large element of a woman's physiologic function, as represented by her sexual organs, reacts on those organs and also on the rest of her body. It is difficult to believe that the endocrine system, so important a part of a woman's economy, can fail to suffer some impairment if the major portion of its function has never been used.

### Journal of Tropical Medicine and Hygiene, London

41: 325-340 (Oct. 15) 1938

- Classification of Certain Groups of Intestinal Bacteria Belonging to the Family Bacillaceae: Tribe Ebertheae and Tribe Encapsulatae. A. Castellani.—p. 325.  
Mycotic Urethritis: Contribution to Study of Nongonorrheal Urethritis. C. Pisacane and A. Coppolino.—p. 332.

### Lancet, London

2: 929-982 (Oct. 22) 1938

- The State and Medical Research. E. Mellanby.—p. 929.  
Meningococcal Meningitis Treated with Proseptasine and Soluseptasine: Record of Nine Cases. R. H. Hannah and F. G. Hobson.—p. 937.  
\*Slowly Fatal Pulmonary Embolism. R. Pilcher.—p. 942.  
Meningo-Encephalitis Complicating Herpes Zoster. J. H. Biggart and J. A. Fisher.—p. 944.  
Severe Initial Deafness as a Sign of Acute Mastoiditis. N. Asherson.—p. 946.

**Slowly Fatal Pulmonary Embolism.**—Pilcher describes a form of fatal pulmonary embolism in which death comes slowly and suggests that such cases should be treated surgically. Four cases are reported, the cause of death being progressive cardiac

failure of acute onset. In two cases embolectomy was attempted, but evidently too late. Embolectomy is suggested as the proper treatment in cases in which improvement does not occur. It should be performed two or three hours after the onset of the illness.

### Archives des Maladies de l'Appareil Digestif, Paris

28: 793-912 (Oct.) 1938

- Perforation of Cancer of Esophagus into Trachea and Bronchi. A. Cain, R. Cattan and H. Silarav.—p. 793.  
\*Value of Atropine Paralysis During Examination of Digestive Tract. A. Bernard and H. Monnier.—p. 806.  
Gastric Syphilis of Pseudoneoplastic Form: Clinical and Radiologic Study. H. Marc and Sire.—p. 813.  
Cancer of Small Intestine. J. M. Noothoven Van Goor.—p. 820.

**Atropine Paralysis During Examination of Digestive Tract.**—Bernard and Monnier employed duodenal dilation by injection of atropine in all roentgenologic examinations of the digestive tract. The technic is as follows: At first the roentgenologic examination of the stomach is made according to the customary method; that is, a series of roentgenograms is made while the patient is standing and reclining. This procedure is followed by the subcutaneous injection of 1.5 mg. of neutral atropine sulfate, and from ten to twenty minutes later a new series of roentgenograms is made while the patient is in the erect and then in the reclining posture. Apart from a certain dryness of the oral mucosa in some instances the authors did not observe any inconvenience from this method. They employed it in seventy-six cases. Summarizing their observations, they state that the injection of atropine in the course of the roentgenologic examination of the digestive tube paralyzes and dilates the stomach, the pylorus, the duodenum, the jejunum and the colon. The transit of barium is retarded and the different organs are well filled and are in an optimal condition of stability for the x-ray film to record their pathologic deformities. Every parietal lesion, neoplasm, ulcer or condition of perigastritis remains uninfluenced by atropine. Consequently the absence of atropine paralysis of a segment of the digestive tube is an indication of an organic lesion. On the other hand, the deformities which disappear under the action of atropine can be considered as of a spasmodic nature. Thus the method permits a definite differentiation between functional and organic disorders. The atropine method brings into evidence more clearly neoplastic lacunas, gastroduodenal ulcers, diverticula and duodenal malformations. Moreover, it involves no danger and merits to be introduced into routine roentgenologic practice.

### Journal de Médecine de Lyon

19: 591-622 (Oct. 20) 1938

- \*Curves of Sedimentation and of Serologic Reactions in Pulmonary Tuberculosis Treated by Pneumothorax: Prognostic Significance. P. Courmont and J. Moulinier.—p. 591.  
Ascorbic Acid (Vitamin C) and Tuberculosis. A.-A. Policard.—p. 611.

**Sedimentation and Serologic Reactions in Pulmonary Tuberculosis.**—Courmont and Moulinier point out that the prognosis of pulmonary tuberculosis must be based on the serologic reactions, especially on the agglutinating power, the deviation of the complement and the bactericidal power in comparison with the clinical factors and with other reactions such as Vernes' resorcinol flocculation and the sedimentation speed. The demonstration of the value of these tests and especially their curve throughout the course of disease is simple in the acute, localized forms which are rapidly cured by pneumothorax treatment; conversely the prognosis is facilitated by these serologic curves. The authors cite the serologic curves of twenty-seven patients who were treated with pneumothorax. In fifteen only the curve of the sedimentation speed was investigated, but in the other twelve all five reactions were studied and especial attention was given to the comparison of the sedimentation speed and the agglutinating power. Some cases were observed for several years, the tests being made frequently, in many instances at monthly intervals, because the prognosis of tuberculosis is estimated in years. Isolated figures of the reactions have less value than the curves, yet an increase in the sedimentation speed and in Vernes' resorcinol reaction has an unfavorable significance at the time they are observed, whereas an

increase of the agglutinating power and of the bactericidal power is a favorable sign. The patients with pneumothorax who have a high agglutinating power are nearly always cured. The curves plotted on the basis of repeated tests and especially their comparison are of especial value. The curves of the sedimentation speed and of Vernes' resorcinol reaction have an analogous significance. They are elevated in the grave periods and at the time when complications develop; they decrease at the time of cure. Their prognostic significance is slight, because it is limited to the present time. The curves of the bactericidal power and especially of the agglutinating power are more important. Their progressive elevation signifies an excellent prognosis; on the other hand, if they are low, and especially if they decrease in the course of pulmonary tuberculosis and of pneumothorax therapy, the prognosis is unfavorable; that is, a fatal outcome may follow within several months. The serologic tests must be evaluated in connection with the clinical, roentgenologic and bacteriologic factors; they are not only helpful in fixing the prognosis but are also valuable in making decisions regarding the conduct and cessation of pneumothorax therapy and in deciding certain surgical interventions (section of adhesions, thoracotomy and so on). The easiest and most demonstrative of the serologic tests for the practice are the sedimentation speed and the agglutinating power, the latter being the most valuable. The comparison of their curves gives the best results, the sedimentation speed indicating the severity of the infection and the agglutinating power the defense of the organism.

### Journal de Radiologie et d'Electrologie, Paris

22: 481-528 (Oct.) 1938. Partial Index

Secondary Electromotor Phenomena of Nerves. A. Strohl and A. Djurno.—p. 481.

\*Anomalies of Vertebral Articular Processes. F. Willemin and M. Cantagrill.—p. 490.

Rapid Evolution of Pulmonary Cyst with Formation of Roentgenograms of Detachment. Brun, Jaubert de Beaujeu and Bège.—p. 495.

Role of Lung and of Pleura in Visibility of Aorta on Transverse Roentgenograms. R. Kirsch and E. Arnold.—p. 501.

Esophageal Diverticulum: Case. Estève.—p. 505.

**Anomalies of Vertebral Articular Processes.**—Willemin and Cantagrill call attention to the difficulties that are encountered by the roentgenologist in the interpretation of spinal roentgenograms. They cite a case in which an anomaly of vertebral articular processes existed which, although rare, may be of great medicolegal significance. The anomaly consists in accessory articular processes on the vertebrae, and the division in the continuity at the level of the vertebral articular processes may lead to confusion with fractures of the articular processes. The patient whose history is reported had accessory articular processes on the second and third lumbar and on the first sacral vertebrae. Following a detailed description of the roentgenologic aspects, the authors review the recent literature on these vertebral anomalies, giving special attention to Wilbur Bailey's report (*THE JOURNAL*, Jan. 23, 1937, p. 266). Bailey found nineteen cases of this anomaly in the literature, six of which presented bilateral lesions. The authors, in addition to the case which they describe and in which the anomaly was detected on three vertebrae, observed another case with an isolated accessory articular process. After citing other opinions on the incidence of the accessory vertebral articular processes, they point out that these abnormal centers of ossification are usually found on the inferior articular processes and that they are exceptionally rare on the superior articular processes.

### Presse Médicale, Paris

46: 1569-1592 (Oct. 26) 1938

Pancreas of Tuberculous Patients. M. Loeper and R. Lesobre.—p. 1569.

\*Treatment of Male Gonorrheal Urethritis. P. Durel.—p. 1571.

**Treatment of Gonorrheal Urethritis.**—Durel discusses the use of various sulfanilamide preparations in the treatment of gonorrheal urethritis. For the treatment of subjects who are not benefited by the local treatment of gonorrheal urethritis he suggests three different possibilities. First he mentions the administration of large doses of 1162 F (*p*-aminophenylsulfanilamide), saying that he has given 4 Gm. a day for five days,

3 Gm. a day for five days and 2 Gm. a day for five days. He emphasizes that this posology requires careful supervision and he does not advise it for routine use. A second possible treatment is the combination of 1162 F in weak doses and 40 R. P. (soluseptazine, that is, disodium-*p*-(gamma-phenylpropylamino) benzenesulfonamide-alpha-gamma disulfonate. The 1162 F is given for seven days in daily doses of 2 Gm., and 20 cc. of soluseptazine is given daily by intramuscular injection. This treatment may cause slight complications and the author does not consider it of great practical interest. The third method suggested is the use of sulfanilamide-pyridine. Following a description of its formula and its behavior in animals, the author describes the clinical results obtained with it. By one method the patient is given 13 Gm. of the medicament in the form of tablets over a period of eight days (two days 3 Gm. each, two days 2 Gm. each, two days 1 Gm. each and two days 0.5 Gm. each). The second method provides 18 Gm. in nine days (3 Gm. for three days, 2 Gm. for three days and 1 Gm. for three days). The third method provides 20 Gm. in eight days (4, 3, 2, and 1 Gm. for two days each). The second type of dosage seems to be suitable in the majority of cases but the author thinks that the future will doubtless modify these methods. Discussing the results obtained with sulfanilamide-pyridine he states that in acute gonorrheal urethritis in males more than 80 per cent of cures were obtained. Of the prolonged cases of urethritis about 70 per cent were cured. In women with metritis of the cervix the results have not been established as yet, but they seem superior to those obtained with other sulfanilamide preparations.

### Schweizer Archiv f. Neurologie u. Psychiatrie, Zurich

42: 1-208 (No. 1) 1938. Partial Index

\*Little's Disease and Epilepsy. M. Biro.—p. 1.

Individual Preparation for Collective Occupational Therapy in Patients with Severe Chronic Schizophrenia. M. Boss.—p. 15.

Action of Insulin on Normal Organism. J. Druey.—p. 27.

After-Examinations of Patients with Dementia Paralytica Who Underwent Malaria Therapy. F. Escher.—p. 37.

Sources of Querulity. A. Kielholz.—p. 58.

Determination of Tryptophan in Cerebrospinal Fluid and Its Results. M. Kraus and K. Mezey.—p. 77.

Appearance of Schizophrenic Exacerbation After Psychic Trauma. R. Mayer.—p. 88.

**Little's Disease and Epilepsy.**—Biro directs attention to the fact that epileptic attacks develop as accompanying symptoms of various disorders. He investigated the epileptic attacks that occur in patients with Little's disease. He says that not all convulsive attacks that occur during Little's disease can be regarded as epileptic but that attacks of an epileptic character do occur in this disease. He observed them in ten of thirty-five patients with Little's disease. The attacks usually developed during the early part of the disease. In some of the cases they preceded the other symptoms by from 3.6 to ten months, in others by only one or two days and in still others they appeared simultaneously with the symptoms of the disease. Irrespective of their time of appearance, they ceased in some of the patients during the further development of the disorder; in others they continued, with intervals, for weeks, months or years. The fact that epilepsy appears in the form of attacks proves that physiologic secondary effects are involved. Endocrine disturbances in women, in whom the attacks recur monthly, and disturbances in the intracranial pressure occasionally make it possible to detect a parallelism between those disturbances and the epileptic attacks. The frequent occurrence of the attacks during sleep, that is, during a periodic process, as well as the intermittent character of the epilepsy may be connected with the sympathetic centers in the diencephalon. In the cases reported by the author, the epileptic attacks occurred during the hemiplegic as well as during the diplegic syndrome, in which pyramidal, extrapyramidal and mixed disturbances predominated. Among the patients with Little's disease who had epileptic attacks there were many who also had psychic disturbances. However, the incidence of the psychic disturbances was not higher than in other patients with Little's disease. In many of the cases of Little's disease with epileptic attacks, no anatomic basis could be found for the attacks. It is difficult



to make a definite prognosis regarding the reappearance of the attacks, even after prolonged observation. The treatment of the epileptic attacks in Little's disease should be like that of cryptogenic or of jacksonian epilepsy.

### Rivista di Clinica Pediatrica, Florence

36: 961-1056 (Nov.) 1938

Nitrogen Metabolism and Utilization of Food by Infants Artificially Fed by Diet Constituted by Vegetal Proteins. A. Bieher.—p. 961.

\*Influence of Lecithin and Lutein on Hypoglycemic Action of Insulin in Diabetes Mellitus. G. Pavan and C. Moro.—p. 994.

**Lecithin and Lutein in Diabetes.**—Pavan and Moro studied the influence of lecithin and lutein on the hypoglycemic action of insulin. In sixteen normal children and six normal rabbits the authors induced hyperglycemia by means of the administration of sugar and followed the behavior of hyperglycemia in the course of a test which consisted in the administration of an intramuscular injection of insulin alone, a lecithin and lutein preparation alone, lutein alone or insulin in association with any of the substances mentioned. In four children who were suffering from diabetes (mellitus or renal) the behavior of glycemia was followed after administration of either insulin alone, the lecithin and lutein preparation alone or insulin in association with this preparation. The authors found that the lecithin lutein preparation has a hypoglycemic action in normal children and in normal rabbits. Lutein has a slight hyperglycemic action, which is due to the fact that the substance on the market contains cholesterol. The lecithin lutein preparation when it is administered to children who are suffering from diabetes either after insulin or in association with it increases the therapeutic action of insulin, makes easy, slow and continuous assimilation of the drug by the patients, acts on the glycemia for several hours and thus prevents hypoglycemia. When insulin in association with the lecithin and lutein preparation is administered for about a month to patients suffering from diabetes, the figures of glycemia during fasting diminish. The dose of insulin can be reduced by this time. According to the authors, lecithin and lutein in diabetic patients stimulate transformation of dextrose into glycogen and also the capacity of the liver and muscles for storing glycogen.

### Annaes Brasileiros de Gynecologia, Rio de Janeiro

4: 311-416 (Oct.) 1938

Hypophysis and Genitalia. C. Salgado.—p. 311.

\*Estrogenic Substance in Treatment of Vulvovaginitis in Little Girls. L. Hoeppner Dutra.—p. 326.

**Vulvovaginitis in Little Girls.**—Hoeppner Dutra reports satisfactory results from the administration of estrogenic substance (progynon B) in the treatment of vulvovaginitis in twelve girls ranging in age from 2 to 10 years. The condition was gonorrheal in ten cases. The substance is given in intramuscular injections, once a week, at a dose of 10,000 international B units (U. B. I.) up to a total number which varies from one to three (and in rare cases four) injections. A vaginal lavage of a 1 per thousand protein silver solution is administered with a short fine sound every other day during the treatment. The mothers of the patients are instructed to put the patients in a sitz bath of tepid water for a few minutes every night. Generally the discharge stops and the gonococcus disappears from the secretion after the third injection. The evolution of the condition is controlled by making weekly examinations of smears prepared from the vaginal discharge. As the treatment advances the number of leukocytes and pus cells diminish in the secretion, the cells of the vaginal epithelium become vacuolar and cornified and the flora of the secretion becomes normal. In two of the cases seen by the author there was a complication of gonorrheal conjunctivitis which was rapidly controlled by the proper local treatment under the influence of the estrogenic treatment. The latter has an average duration of three or four weeks. It is not followed by complications. Recovery of the patients is permanent. According to the author the estrogenic treatment has a biologic action by which a cellular proliferation of the vaginal epithelium is stimulated, the reaction of the vaginal discharge is favorably modified (acidity) and the vaginal mucosa is regenerated.

### Archiv für Gynäkologie, Berlin

167: 397-654 (Oct. 10) 1938. Partial Index

\*Respiration and Capacity of Blood to Bind Oxygen During Pregnancy. W. Borgard and G. Effkemann.—p. 397.

Determination of Estrogenic Hormone in Blood and Urine During Delivery (Significance of Follicular Hormone to Delivery). G. Tsutsumopoulos.—p. 403.

\*Latent Period of Incipient Cervical Carcinoma and Duration of Freedom from Symptoms. E. Scipades Jr. and K. S. Stevenson.—p. 416.

Behavior of Genital Apparatus of Female Rats During Prolonged Administration of Estrogen. Käthe Biedermann.—p. 465.

Hormonal Etiology of General Fetal Dropsy. E. Tschern.—p. 489.

Modification of Vaginal Epithelium in Child by Means of Estrogen: Dosage of Estrogen in Gonorrheal Vaginitis in Children. K. Herrberger.—p. 506.

**Respiration and Blood Oxygen During Pregnancy.**—During pregnancy, according to Borgard and Effkemann, respiration is altered in two respects: 1. As a result of the elevation of the diaphragm, the deep inspiration is mechanically impaired, the volume of the individual respiration is reduced and as a compensation the respiratory frequency is increased. 2. The total extent of the ventilation, the respiratory minute volume is greater than corresponds to the increased oxygen requirements of pregnancy (increase of basal metabolism during pregnancy). It has been pointed out repeatedly that the respiratory minute volume is increased by from 10 to 20 per cent during pregnancy. The authors subjected pregnant women to work tests in order to determine whether work requires a percental increase in the respiration compared to normal conditions and to what extent a changed oxygen combining power of the blood influences the respiratory minute volume. In a table the authors show the results which they obtained in twenty-seven tests. A comparison with the normal values of nonpregnant healthy women revealed that, with the same exertion, the respiration of pregnant women is considerably greater, although the absorption of oxygen per time unit is reduced as a sign of the decreased circulatory capacity during pregnancy. These quantitative determinations seemed necessary as a foundation for the investigation as to why the ventilation is increased during pregnancy. It was found that the increase in ventilation is due to an impairment of the conditions of arterialization in the blood. The curve recording the oxygen combining power of the blood of pregnant women is displaced toward the right even during rest; that is, a higher oxygen tension in the alveolar space is required than is the case in the absence of pregnancy. During exertion, the curve of the oxygen binding power of pregnant blood is essentially more toward the right than that of nonpregnant women.

**Latent Period of Incipient Cervical Carcinoma.**—In this extensive report, Scipades and Stevenson review the literature on the problem of the beginning cervical carcinoma and report their own extensive studies. Summarizing their observations, they say that on the basis of cases that were selected from a clinical material over a period of twenty years it can be stated that the incipient cancer passes through a period in which there are no symptoms and the growth is not progressive. This latent period lasts at least six months and it may last six or even eight years, the average being about 3.9 years. The authors observed further that the carcinomas, which were detected early by means of exploratory excisions and which were treated by extirpation of the cervix, by radium irradiation or a combination of the two methods were always cured. Finally the authors demonstrated that the hyperactive epithelial changes can be regarded neither as precancerous conditions nor as incipient cancers, because they never developed into cancers. They gained the impression that these epithelial changes, just like the leukoplakias of the cervix, are fluctuating manifestations which, under the influence of different factors, may develop and disappear again. They say that it has been asserted that the surgical as well as the radiation therapy of the completely developed carcinoma has reached the limits of its possibility. They show that, if this is so, the only hope for further improvement is the earlier recognition of the carcinoma and they believe that the test developed by Schiller (staining with compound solution of iodine) and the colposcope devised by Hinselmann are valuable aids in facilitating an early diagnosis.

**Klinische Wochenschrift, Berlin**

17: 1457-1496 (Oct. 15) 1938. Partial Index

- Action on Renal Function of Substances that Increase Blood Pressure. D. Schneider and P. W. Springorum.—p. 1460.
- Antithyrotropic Protective Power of Blood of Healthy Persons and Patients. H. Eitel.—p. 1465.
- Splenomegaly Verified as Boeck's Disease by Means of Sternal Puncture: Case. M. Dressler.—p. 1467.
- Mode of Action of Prostigmine in Myasthenia Gravis. A. Lanari.—p. 1471.
- \*Nature and Diagnostic Significance of Triboulet's Reaction. H. Wiesbrock.—p. 1473.
- Significance of Culture of Bone Marrow for Demonstration of Bacilli of Typhoid and of Paratyphoid. A. Ott.—p. 1475.
- Differentiation of Whooping Cough Bacilli and Influenza Bacilli. A. Steigler.—p. 1480.

**Triboulet's Reaction.**—Wiesbrock points out that Triboulet's reaction is used chiefly for the diagnosis of intestinal tuberculosis but that, although it produces positive reactions in all cases of intestinal tuberculosis, it results in such reactions also in a large number of disorders and therefore cannot be regarded as specific for intestinal tuberculosis. In studies on seventy-four patients in whom intestinal tuberculosis was suspected, the author gained the impression that the protein bodies are demonstrable in the intestine in especially severe infections and intoxications. In order to throw more light on this problem, he made Triboulet's test on all specimens of feces, 550 in all, which were submitted to him for bacteriologic examination in order to detect typhoid, paratyphoid or dysentery. In this material seventeen cases of typhoid were detected and the positive bacteriologic test was accompanied by a positive Triboulet reaction. In thirty-five cases of paratyphoid, in ten cases in which bacilli of the Breslau type were found, in sixteen of dysentery, in fourteen bacillus carriers and in a number of cases negative to bacteriologic examination Triboulet's reaction was found to be positive. It was also noted (although not always) that Triboulet's reaction produced a somewhat different type of precipitation in dysentery than it did in paratyphoid. Whereas the latter usually yielded a coarse precipitate and a clear supernatant fluid, the precipitate of dysentery often showed a fine granulation and a more or less clear supernatant fluid. Thus it was frequently possible to foretell the outcome of the bacteriologic test from the results of Triboulet's reaction. The author thinks that, if his observations should be corroborated by others, Triboulet's reaction could be employed as a diagnostic aid in infectious diseases of the intestine. The bacteriologic examination is often difficult, because bacilli are not always excreted with every stool. The author thinks that in large material it might perhaps be advisable first to subject the stools to Triboulet's test and then to make bacteriologic tests only on specimens in which Triboulet's reaction proves positive.

**Münchener medizinische Wochenschrift, Munich**

85: 1617-1656 (Oct. 21) 1938. Partial Index

- Cardiovascular Xanthomatosis as Cause of Death in Young Persons: Contribution to Forms of Lipoidoses. H. Siegmund.—p. 1617.
- \*Pregnancy Polyneuritis and Its Relation to Vitamin B<sub>1</sub>. A. Hildebrandt and H. Otto.—p. 1619.
- Treatment of Lambliasis with Atabrine. K. Heilmann.—p. 1626.
- Prevention of Infection After Accidental Injuries. C. Fervers.—p. 1628.
- Occupational Arsenic Intoxications in Wine Growers. W. Frohn.—p. 1630.
- Bullous Pulmonary Emphysema After Relapsing Infarct Pneumonia as Result of Accident. K. Bühler.—p. 1636.
- Coxa Vara, Its Clinical Aspects and Treatment. M. Lange.—p. 1637.

**Pregnancy Polyneuritis and Vitamin B<sub>1</sub>.**—Hildebrandt and Otto direct attention to the fact that treatment with vitamin B<sub>1</sub> is of great value in the polyneuritis of pregnancy. They report the clinical history of a woman who developed a severe polyneuritis during pregnancy. They instituted treatment with vitamin B<sub>1</sub> and vitamin C. The woman received during her pregnancy a total of 1,782 mg. of vitamin B<sub>1</sub> and there were no disturbing secondary effects such as premature elicitation of labor pains or symptoms of excessive dosage. The pregnancy terminated in the birth of a healthy child. Tests on the urine of the woman disclosed that up to the delivery no vitamin B<sub>1</sub> was eliminated in the urine and vitamin C was excreted in small quantities. Later, however, nor-

mal secretion was observed and vitamin B<sub>1</sub> could be detected in the serum. Not only did the administration of vitamin B<sub>1</sub> improve the pregnancy polyneuritis but the subacidity of the gastric juice and the hypochromic anemia were counteracted; the fasting blood sugar was slightly influenced (temporary slight decrease) and a hepatic disturbance was compensated. The authors conclude that, in the presence of severe paralytic symptoms during pregnancy, treatment with vitamin B<sub>1</sub> should always be tried before an interruption of the pregnancy is decided on.

**Zeitschrift für Urologie, Leipzig**

32: 649-720 (No. 10) 1938. Partial Index

- Peridural Anesthesia. C. E. Alken.—p. 649.
- \*Phosphate Concrements of Urinary Tract. A. T. Jensen and J. E. Thygesen.—p. 659.
- Therapy of Chronic Urinary Retention of Bladder (Hypertrophy of Prostate) with Transurethral Resection of Prostate. I. Farkas.—p. 667.
- Combined Vesicovaginal and Uterovaginal Fistula. E. Michadovski.—p. 680.
- Roentgenokymographic Investigations on Normal and Abnormal Motility of Excretory Urinary Passages. M. Maintz, J. Meese and G. Wüllenweber.—p. 682.
- Hypernephroma of Right Half of Horseshoe Kidney. G. Nicolich.—p. 696.
- Pyocaneus Osteomyelitis of Vertebral Column Following Pyelonephritis: Case. T. Kusunoki.—p. 699.

**Phosphate Concrements of Urinary Tract.**—Jensen and Thygesen discuss recent developments in the chemistry of calcium phosphates and describe their studies on thirty-five phosphate calculi that had been obtained in renal and vesical operations and in the course of necropsies. In the qualitative analysis, sections of the calculi were pulverized and 0.25 Gm. of this powder was examined for carbonate, ammonia, phosphate, oxalate calcium and magnesium and in some cases also for uric acid and albumin. The analyses were always made in the same manner and the reactions were compared among one another and with the reactions of known quantities of pure substances. This method permits a rough estimate of how much of the various substances is contained in the calculi. The authors give an example of such an analysis. Further, roentgenologic diagrams were made of the pulverized calculi. These diagrams were then compared with the results of the analyses. In a few instances, diagrams were made also of the residue on ignition. The authors detected the following substances in the calculi: (1) magnesium ammonium phosphate, (2) a colloid-like calcium phosphate with incomplete apatite structure, which contains between three and three and one-half equivalents of calcium per mol of phosphoric acid and some closely bound water, and (3) beta-tricalcium phosphate. Those mentioned under points 1 and 2 are the usual constituents of phosphate calculi and they are found more frequently mixed than pure. Two calculi consisted of beta-tricalcium phosphate. So far it has not been possible to extract beta-tricalcium phosphate from aqueous solution but only by direct reaction between calcium oxide (CaO) and phosphorus pentoxide (P<sub>2</sub>O<sub>5</sub>) under high temperature. Calcium carbonate, normal magnesium phosphate and the secondary calcium phosphates, which are often designated as the usual constituents of phosphate calculi, were not detected.

**Maandschrift voor Kindergeneeskunde, Leyden**

7: 461-501 (Sept.) 1938

- \*Bacillary Dysentery in Young Nurslings. B. Lammerts van Bueren and J. H. de Haas.—p. 461.
- Cases of Suprarenal Virilism. J. H. Smidt van Gelder.—p. 472.
- Icterus Gravis: Case. J. H. Smidt van Gelder.—p. 478.
- Klippel-Feil Syndrome: Case. A. van Westrienen.—p. 486.
- Mucineal Manifestations in Presence of Ascarides. C. J. Wijckerheld Bisdorf.—p. 490.

**Bacillary Dysentery in Young Nurslings.**—Lammerts van Bueren and de Haas report that among 400 children with bacillary dysentery observed at the children's clinic in Batavia there were 160 nurslings and eleven of these were less than 3 months old. On the basis of the clinical observations on these eleven young nurslings and of the bacteriologic examination of their feces, the authors conclude that bacillary dysentery may attack nurslings during the first three months of life, irrespective of whether they are bottle fed or breast fed. The course of the bacillary dysentery in these young nurslings is changeable and may even be fatal, just as in older children. Regarding

the etiology, the authors say that in the nurslings of the first quarter of life the same bacilli, the so-called pseudodysenteric bacilli, are encountered that are found also in the older children with bacillary dysentery. The dysenteric character of the feces is usually less pronounced in the young nursling than in older children. The diagnosis of bacillary dysentery requires the microscopic examination of the feces in the young nurslings as in the older children. It reveals a greater or lesser number of leukocytes and a few or no erythrocytes. The treatment of bacillary dysentery should be dietetic even in the young nurslings. Little or no medicaments should be given.

### Acta Pædiatrica, Stockholm

23: 1-140 (Oct. 15) 1938

- Comparison of Organic Acids and Sulfanilamide as Urinary Antiseptics. H. F. Helmholz.—p. 1.  
White Blood Picture During First Year of Life, Especially with Regard to Its Course. J. H. Magnusson.—p. 14.  
\*Investigations of C Vitamin Standard in Healthy Children and in Children Suffering from Gingivitis. C. W. Herlitz.—p. 43.  
Neuroblastoma in Left Adrenal with Intrathoracic Metastases. J. Reurink.—p. 78.  
Experimental Studies on Conditioned Salivary Reflexes in Children. C. G. Bernhard.—p. 118.  
Undesirable Tuberculin Reactions. II. Behrendt.—p. 129.

**Investigations of Vitamin C.**—Herlitz used the modified Lund and Lieck method of determining the content of ascorbic acid in the blood serum in forty-four healthy children without gingivitis and fifty-seven children with severe gingivitis, between the ages of 3 and 16 years, after the oral administration of 10 mg. of ascorbic acid per kilogram of body weight. It was found that the ascorbic acid content of the serum increased in the same degree to which raw fruit was added to the diet. This signifies an indirect control of the reliability of the food anamneses. The average fasting value for children who were given a moderate supply each day of raw fruit (approximately one orange or apple) in addition to an otherwise normal diet was  $0.71 \pm 0.073$  and the two hour value, after loading, was  $1.87 \pm 0.111$  mg. per hundred cubic centimeters of serum. The corresponding figures for children who, under otherwise similar conditions, seldom or at most received raw fruit only once a week were  $0.24 \pm 0.025$  and  $0.69 \pm 0.05$  mg. respectively. When the fasting values lie below 0.4 and, simultaneously, the two hour value is below 1 mg. the child has probably been receiving food poor in vitamin C content or a subnormal vitamin C standard is present. The existence of this combination of values does not in itself permit the diagnosis of scurvy. The probability that gingivitis has any connection with subnormal ascorbic acid was not elicited but that this condition must be referred to some other etiologic factors is suggested. Extremely low serum-ascorbic acid values may be made to rise to a normal level in three weeks by adding fruit to the diet in moderate amounts.

### Ugeskrift for Læger, Copenhagen

100: 1069-1090 (Sept. 22) 1938

- \*Simple Urethritis or "Catarrh of Urethra": Comparative Experiences and Considerations on This Disease and Gonorrheal Urethritis. V. Genner.—p. 1069.  
\*Treatment of Infections of Urinary Tract with Calcium Mandelate: One Year's Experiences. E. Schnohr and C. Johansen.—p. 1074.  
Infections of Urinary Tract Treated with Granulate of Calcium Mandelate. K. Rasmussen.—p. 1082.

**Simple Urethritis and Gonorrheal Urethritis.**—Genner says that, while simple urethritis in women is hardly as rare as commonly thought, his comparative statistics on this disorder and gonorrheal urethritis in more than 100 cases in men show a frequency ratio of 1 to 2. He asserts that the form of simple urethritis designated as "postgonorrheal catarrh" now constitutes only a small percentage of the total number of cases; its probable greater frequency formerly is ascribed to the more irritative treatment of gonorrhea then used. In about one third of the cases of simple urethritis there was history of earlier gonorrhea, but as a rule far back and without direct connection with the simple urethritis. Sulfanilamide seems to him an important addition to treatment.

**Urinary Tract Infections Treated with Calcium Mandelate.**—Schnohr and Johansen used calcium mandelate in the treatment of sixty patients with infections of the urinary tract. The dose was 12 Gm. daily and the amount of fluid ingested

was limited to 1 liter daily. In thirty-nine cases the urine became sterile, in thirty-one after a week or less, in five after from nine to thirteen days, in three after twenty, twenty-five and sixty-five days respectively. In thirteen cases the subjective symptoms disappeared although the urine did not become sterile. The treatment was without effect in eight cases (six with complicating disorders, one with a history of ureterotomy, one in a pregnant woman given only two days' treatment). The urine became sterile in seven of twenty patients in whom the infection was a complication in a grave disorder of the urinary tract and in eight of thirteen cases with milder complications. The bacillary infection was eliminated in thirty-four of forty-seven cases with *B. coli* infection, in two of nine cases with *B. proteus* infection and in some cases with infection with staphylococci, gram-positive cocci and hemolytic streptococci. In most cases the  $pH$  in the urine was reduced to between 4.8 and 5.3. As a rule the urine did not become sterile until the  $pH$  was 5.3 or less, it was never sterile when the  $pH$  was over 5.5. In six cases in which the  $pH$  remained between 6 and 8 the addition of from 3 to 6 Gm. of ammonium chloride daily brought the  $pH$  to about 5 in four and the urine became sterile in two. Except for a transitory hematuria in one instance, treatment with calcium mandelate caused no injurious effect on the kidneys although the renal function was impaired in several cases. Only two patients were unable to take the granulate because of gastric symptoms. Occasionally nausea occurred after some days' treatment, and in two cases there was nausea during the first days.

100: 1091-1126 (Sept. 29) 1938

- \*Osteomalacia of Spinal Column in Denmark in Cases with Deficient Diet or Diseases of Alimentary Tract. E. Meulengracht.—p. 1091.  
Condition of Teeth at Bornholm. II. C. Olsen.—p. 1116.  
Contact Ulcer. G. Hagerup.—p. 1117.

**Osteomalacia of Spinal Column.**—Meulengracht reports eighteen cases of osteomalacia in which the changes were localized chiefly in the spinal column. The subjective symptoms were pain in the back and groins, occasionally in acute attacks (spontaneous fractures). External examination established a settling of the back sometimes with kyphosis or lordosis. Often there was considerable decrease in height. Roentgen examination showed calcium deficiency in the skeleton, most marked in the spinal column; the vertebrae were low, biconcave or more irregularly deformed. Sometimes there was also a roentgenologically demonstrable osteo-arthritis of the spinous process (Baastrup's disease) in the lumbar region, originated through the settling and shortening of the lumbar column. The changes are in some of the cases attributed to diet deficient in calcium and vitamin D; in the other cases gastric achylia or misuse of laxatives is believed through changed conditions of resorption to have been the contributing cause or the main cause for the development of the symptoms. Treatment with calcium salts and vitamin D proved effective.

### Uppsala Läkareförenings Förhandlingar, Uppsala

43: 267-464 (June 30) 1938

- \*Effect of Dextrose on Tar Tumors in Mice. K. A. Vannfält.—p. 267.  
Roentgen Symptoms in Abdominal Injuries through Blunt Force. II. Laurell.—p. 413.

**Effect of Dextrose on Tar Tumors in Mice.**—Vannfält studied the effect of feeding 50 per cent dextrose solution on the growth and metastasis of tar tumors in mice and the length of life of the animals. In the females given dextrose there was a statistically established checking of metastases to the regional lymph nodes and to the lungs. In the mice with cancerous skin tumors the control group showed a statistically greater frequency of metastases (without regard to their localization) than the mice fed dextrose. The resistance of the animals with malignant tumors which expresses itself in greater length of life is considered a biologic indicator of the degree of malignancy. Since the animals given dextrose lived longer, the author thinks it probable that the tumors were less malignant than in the control group. Investigations on the effect of insulin on tar cancers in mice indicated that in the daily dose of 0.02 clinical unit it exerted no certain influence on the time of appearance of the tumor, its malignant degeneration or metastasis to the regional lymph nodes or internal organs but shortened the lifetime of the animals.

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## ALLERGY IN CHILDHOOD

### III. ITS ONSET AND NATURAL PROGRESS

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NEW YORK

Many factors that enter into the problem of the initiation of allergy have been considered in a previous paper of this series in which the various modes of acquisition were treated.<sup>1</sup> Here attention will be directed mainly to certain observations relative to the early beginnings and the natural course that allergy follows with increasing age. I have limited my observations to the four major syndromes eczema, asthma, hay fever and urticaria. A correlation of such observations, I believe, will help in the early diagnosis of these conditions and, if properly treated, should tend to abort further progress of the allergic syndromes.

#### THE ONSET

Practically all students concerned with allergy in adults find that from 50 to 60 per cent of their patients give a history of onset in childhood. The early careful observations of the beginnings of allergy, however, were first made by pediatricians, among whom should be mentioned Schloss,<sup>2</sup> Talbot<sup>3</sup> and Blackfan.<sup>4</sup>

In a series of 250 allergic children, my associates and I found that 50 per cent had symptoms in the first year; by the fifth year 80 per cent manifested syndromes, and between the eighth and tenth years allergy was already established in practically all our patients.

A direct approach to the study of the onset of allergy can best be served by an analysis of the group of allergic infants who were under 1 year of age. The family history was positive in only 52 per cent of the cases, indicating that there are just as many infants without an allergic family history who have an early onset of allergy as those with a positive history.

Cooke and his co-workers<sup>5</sup> adduced from their studies that the greater the degree of inheritance, the earlier will be the onset of allergic phenomena. The studies of Cooke, however, were largely concerned with

adults, the majority of whom suffered from hay fever. Studies on asthma by Bray,<sup>6</sup> Peshkin<sup>7</sup> and O'Keefe<sup>8</sup> dealing exclusively with children and our own observations on general allergy in childhood lead us to conclude that the age of onset is not as strongly influenced by heredity as is generally believed. It cannot be denied that there are more affected children in a small percentage of families (in our series in about 12 per cent) with a strong familial allergic tendency than in those in which this tendency is absent. While one may have to admit that a greater susceptibility for allergy does exist in certain children, it does not appear that the actual age of onset is influenced solely by genetic factors.

In the infants under 1 year of age, eczema was the presenting syndrome in 90 per cent. The remaining 10 per cent suffered from asthma. Though of the cases recorded the youngest patients with asthma were respectively 14 and 28 days old,<sup>9</sup> this early onset apparently is not the rule. Of our patients with asthma under 1 year of age, the average age at onset was 7.3 months. As I shall show presently, however, the overwhelming majority of cases start after the first year. As compared with asthma, there is a striking difference in the age at onset of eczema in infants under 1 year, which was 1.9 months. It is also interesting to note that the average age at the time of observation was 6.5 months for the patients with eczema and 9.6 months for patients with asthma under 1 year. It is apparent from these figures that eczema is the prevailing allergic condition in infancy and that it starts considerably earlier than any other syndrome. This is not a signally new observation; as a matter of fact, it is generally accepted as being axiomatic.

We found a surprisingly high degree of cutaneous reactivity among our patients under 1 year.

Some of the youngest patients for whom positive cutaneous reactions were reported were those of Balyeat,<sup>10</sup> who tested 119 normal newborns with egg, milk and wheat at 3 days of age. For one infant he obtained a four plus reaction to wheat which lasted one hour and ten minutes. Another gave an unquestionable three plus reaction to egg which persisted for fifty minutes. Smyth and Bain<sup>11</sup> found no positive reactions among 125 normal newborns. This is not surprising, for Peshkin and Rost<sup>12</sup> found only 10 per cent doubtful

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Read before the Section on Pediatrics at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

1. Ratner, Bret: Allergy in Childhood: I. The Modes of Its Acquisition, *J. Pediat.* **12**: 730 (June) 1938.

2. Schloss, O. M.: A Case of Allergy to Common Foods, *Am. J. Dis. Child.* **3**: 341 (June) 1912.

3. Talbot, F. B.: Idiosyncrasy to Cow's Milk; Its Relation to Anaphylaxis, *Boston M. & S. J.* **175**: 191 (Aug. 10) 1916.

4. Blackfan, K. D.: A Consideration of Certain Aspects of Protein Hypersensitiveness in Children, *Am. J. M. Sc.* **160**: 341 (Sept.) 1920.

5. Cooke, R. A., and Vander Veer, A.: Human Sensitization, *J. Immunology* **1**: 201 (June) 1916. Spain, W. C., and Cooke, R. A.: Studies in Specific Hypersensitiveness: XI. The Familial Occurrence of Hay Fever and Bronchial Asthma, *J. Immunol.* **9**: 521 (Nov.) 1924.

6. Bray, G. W.: Recent Advances in Allergy, ed. 2, Philadelphia, P. Blakiston's Son & Co., 1934.

7. Peshkin, M. M.: Asthma in Children: IV. Hypersensitiveness and Family History, *Am. J. Dis. Child.* **36**: 89-101 (July) 1928.

8. O'Keefe, E. S.: An Analysis of Three Hundred Cases of Asthma in Children, *New England J. Med.* **214**: 62-65 (Jan. 9) 1936.

9. Salter, Hyde: Asthma, New York, William Wood & Co., 1882.

10. Balyeat, R. M.: The Hereditary Factor in Allergic Diseases, *Am. J. M. Sc.* **176**: 332 (Sept.) 1928.

11. Smyth, F. S., and Bain, Katherine: The Direct Skin Test in Allergy, *J. Allergy* **2**: 316-327 (July) 1931.

12. Peshkin, M. M., and Rost, W. L.: Incidence of Protein Sensitization in Normal Child, *Am. J. Dis. Child.* **23**: 51-62 (Jan.) 1922.

or positive reactions in a large group of normal children, the youngest group being between 2 and 5 years of age. Blackfan<sup>13</sup> found only one positive cutaneous reaction among forty-three normal individuals, that one instance occurring in an infant 9 weeks of age.

Balyeat's finding, which must be regarded as extremely fortuitous, however, is of importance, for it indicates that a positive reaction can be obtained in a newborn infant, and it must be presumed, as Balyeat himself suggests, that sensitization must have occurred in utero.

Blackfan reports a positive reaction in an allergic child at 5 weeks, Lyon<sup>14</sup> at 6 weeks, Shannon<sup>15</sup> at 8 weeks and Smyth<sup>11</sup> at 11 weeks. In our own series, we had three eczematous infants, one as young as 9 weeks and two who were 12 weeks old, who showed cutaneous sensitivity. Stuart and Farnham<sup>16</sup> infer that hypersensitivity to food proteins tends to be present at birth.

Positive reactions were obtained in 85 per cent of the patients under 1 year of age. While 100 per cent reacted to foods, only 41 per cent reacted to foods alone, whereas 53 per cent reacted to foods, inhalants and contactants and 6 per cent reacted to these and pollens in addition.

Sensitivity to foods is a common observation of those working with infants. In fact, the preponderance of positive reactions to food tests in the first year has led certain investigators to suggest that the infants become sensitive when these foods are eaten. Smyth<sup>17</sup> aptly takes objection to this point of view. Egg white, which stands first in order of frequency in positive reactions, is not introduced into the diet as early, nor in the same quantity, as is cow's milk, to which many fewer infants react.

Our concept of active intra-uterine sensitization—owing to the passage of undigested food protein from the maternal blood stream to the fetal circulation by way of the placenta—offers a plausible explanation for those cases of food reactors who have never eaten the food prior to being tested, or for those who manifest allergic reactions the first time the food is consumed. This concept, which I<sup>18</sup> voiced in 1928, has corroboration in the earlier observations of Schloss and Worthen,<sup>19</sup> Blackfan<sup>4</sup> and many others, who report cases in which positive reactions to egg white were obtained in infants who had never eaten eggs. Schloss<sup>20</sup> observed that in sixteen cases out of thirty-three symptoms developed the first time some food was eaten, and similar cases were also reported by Blackfan.<sup>4</sup>

The preponderance of sensitivity to egg white in these congenitally sensitized infants can be assumed to be due to its consumption by the pregnant woman in relatively large amounts (often in a raw or partially cooked state), to its low molecular weight and to its low coefficient of digestibility.

Even more convincing than infants sensitive to egg are those young infants who react to nuts, fruits and

vegetables, which foods, by the farthest stretch of the imagination, could not be presumed to have been ingested by them.

In the paper written by Lyon<sup>14</sup> in 1928, which appeared shortly after my article on the influence of the antepartum diet on allergy in infancy, a case is described of an infant 3 weeks old in whom angioneurotic edema developed and at 6 weeks cutaneous reactions to corn and navy beans were positive. The mother gave negative cutaneous reactions. In his paper the author stressed only the possibility that these antigens had come through the breast milk. My interest was aroused by the case and, in subsequent correspondence, I learned from Dr. Lyon that the family lived in the inaccessible rural mountain regions of West Virginia. At times the natives live almost exclusively on corn bread and dried navy beans. He further stated that the mother of the patient subsisted on such a bizarre diet for the last ten weeks of her pregnancy; prior to that time she had partaken of a reasonably good diet. It seems doubtful that the infant could have been sensitized in so short a time from the minute amounts of foreign protein in the breast milk. The more plausible explanation, it seems to me, is that the infant was sensitized in utero.

Another point of interest is that the angioneurotic edema was more probably due to contact of the mother's hands than to the breast milk. This woman made her own corn bread and her hands may have been contaminated with the food proteins, which were thus brought in direct contact with the mammary glands and the infant's skin.

This remarkable case emphasizes the need for testing even young infants with food proteins other than egg, wheat and milk to which many investigators have limited themselves.

Intra-uterine sensitization by no means explains all the cases. Only 55 per cent of our infants gave evidence of such initiation of sensitivity. The remaining 45 per cent must have acquired food sensitivity after birth. Milk and wheat proteins are the early prime offenders. The studies of Schloss<sup>21</sup> so clearly demonstrate the mechanism of intestinal permeability to foods in malnourished and normal infants that the validity of this form of acquisition is unquestioned.

Analysis of a case of idiosyncrasy to milk cited by Talbot<sup>3</sup> can be used to exemplify the development of postnatal sensitization.

A healthy, exclusively breast fed baby at 8½ months of age was given one bottle of milk formula. This was not given again until three weeks later because the baby had an infection of the middle ear. After recovery the milk formula was tried again but refused by the baby. It was, therefore, fed to him by spoon, but he vomited it. Several further attempts were made to give milk or whey, but vomiting ensued each time. Breast feeding was resumed for one week and was tolerated. Subsequently, 1 ounce (30 cc.) of milk was put into 8 ounces (240 cc.) of cereal gruel and only one teaspoonful of this mixture was given. The baby shuddered and vomited, and within an hour his body was covered with an urticarial eruption. The child was put on goat's milk without further trouble. Six months later, cow's milk was resumed and tolerated.

The factors influencing this mode of sensitization are covered more fully in part II of this series<sup>22</sup> and cannot be gone into at greater length here.

13. Blackfan, K. D.: Cutaneous Reactions from Proteins in Eczema, *Am. J. Dis. Child.* **11**: 441 (June) 1916.

14. Lyon, G. M.: Allergy in an Infant of Three Weeks, *Am. J. Dis. Child.* **36**: 1012 (Nov.) 1928.

15. Shannon, W. R.: Eczema in Breast Fed Infants as a Result of Sensitization to Foods in the Mother's Diet, *Am. J. Dis. Child.* **23**: 392-405 (May) 1922.

16. Stuart, H. C., and Farnham, Marynia: Acquisition and Loss of Hypersensitiveness in Early Life, *Am. J. Dis. Child.* **32**: 341-349 (Sept.) 1926.

17. Smyth, F. S.; Bain, Katherine M., and Stallings, Minnola: Infantile Eczema, *J. A. M. A.* **97**: 1291-1294 (Oct. 31) 1931.

18. Ratner, Bret: A Possible Causal Factor of Food Allergy in Certain Infants, *Am. J. Dis. Child.* **36**: 277-288 (Aug.) 1928.

19. Schloss, O. M., and Worthen, T. W.: The Permeability of the Gastro-Enteric Tract of Infants to Undigested Protein, *Am. J. Dis. Child.* **14**: 342 (May) 1916.

20. Schloss, O. M.: Allergy in Infants and Children, *Am. J. Dis. Child.* **19**: 433-454 (June) 1920.

21. Schloss, O. M.: The Intestinal Absorption of Antigenic Protein, *Harvey Lectures*, series 20, 1924-1925, p. 156.

22. Ratner, Bret: Allergy in Childhood: II. Prophylaxis, *J. Pediatr.* **12**: 737 (June) 1938.

Although so much stress has been laid on the dominance of sensitivity to egg, which we found in 67 per cent of our cases, this substance could not have been the cause of the allergic manifestation in the infants who were not receiving it in their diet. If egg is not the provocateur of an eczema in the very young and is merely indicative of a potential sensitivity, and if, at the same time, one finds positive reactions to environmental substances, then obviously the latter substances must be causally related to the eczema. Practically in all these cases there was multiple sensitivity (94 per cent). It has been thought that inhalants and contactants begin to play their role much later than foods, but we did not find it so in our patients under 1 year of age; as I have already noted, 53 per cent reacted to inhalants and contactants in addition to foods, and 6 per cent to pollens in addition.

In table 1 are listed some of the reactions obtained in these young infants. As will be noted in several instances, the inhalant-contactant group is the major offender even though reactions to foods are positive. The articles of Peck and Salomon,<sup>23</sup> Hopkins and Kesten,<sup>24</sup> Hill and Sulzberger<sup>25</sup> and others emphasize the

childhood, but it is only after the sixth year that the incidence of fixed hay fever becomes notable. It is well known that the major number of hay fever sufferers commence their symptoms after puberty, the second decade being the most vulnerable period. However, one cannot be too dogmatic about it, for our studies pertain to the middle Atlantic states, and it must be acknowledged that workers in the great Southwest believe that

TABLE 2.—Age of Onset and Duration of Various Syndromes Before Seen

	Age of Onset	Duration Before Seen for Allergy	Average Age of Patient when Seen for Allergy
Eczema.....	0.7 years (3 days-5½ yrs.)	1.8 years (1 wk.-11.9 mos.)	2.5 years
Asthma.....	3.6 years (2 mos.-13 yrs.)	3.6 years (0-14 years)	7.2 years
Hay fever....	7.9 years (9 mos.-13½ yrs.)	3.9 years (0-11 years)	11.8 years
Urticaria.....	4.4 years (5 mos.-14 yrs.)	2.3 years (1 mo.-1 year)	6.7 years

Age of onset in eczema-asthma cases: Eczema 0.6 year; asthma 3 yrs.

hay fever may start early in life.<sup>26</sup> Kahn reports that 10 per cent of his patients with hay fever are under 1 year, and in five cases he states that hay fever symptoms existed from birth.

The urticarias appear to jog along sporadically throughout childhood, and, when one recalls the 3 week old infant of Lyon, it is evident that no period is free from this syndrome.

It is of further interest to note (table 2) that the period between the age of onset and the time that medical attention is sought is shortest for eczema (1.8 years) and next in order comes urticaria (2.3 years); the longest periods elapse in the case of asthma and hay fever (3.6 years and 3.9 years respectively). Perhaps because eczema and urticaria are very troublesome and disfiguring patients are brought for treatment earlier than with asthma and hay fever. The latter conditions are difficult to diagnose and sometimes require several years of observation. They are frequently wrongly diagnosed

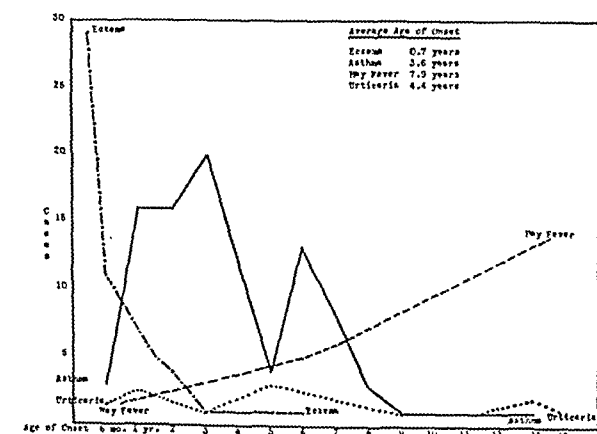


Chart 1.—Showing influence of the allergic syndrome on age of onset.

and treated as common colds, recurrent bronchitis, pneumonia or whooping cough.

The average age of the patient at the time of study is youngest for eczema and oldest for hay fever.

26. Kahn, I. S.: Significance of Negative Skin Tests in Pollen Hay Fever and Asthma in Infants and Young Children: Treatment, *South. M. J.* 21: 559-562 (July) 1928. Balyeat, R. M.: Allergic Manifestations in Children Based on the Study of Four Hundred Eighty-Two Cases, *ibid.* 24: 769-774 (Sept.) 1931.

TABLE 1.—A Group of Cases in Infants Under 1 Year of Age Showing Multiplicity of Sensitivity

Case	Age, Months	Condition	Positive Reactions
1	3	Eczema	Egg, wheat, silk, and environmental substances
2	4½	Eczema	Egg, milk, vegetables
3	5	Eczema	Egg, milk, contactants
4	6	Eczema	Egg, milk
5	6	Eczema	Orange
6	7	Eczema	Egg, apple
7	7	Eczema	Egg, several vegetables, contactants
8	7	Eczema	Egg, contactants
9	9	Asthma	Egg, inhalants and pollens
10	10½	Eczema	Egg, pea, chicken feathers and cotton lintens

important role of environmental substances in the causation of eczema not only through direct contact of the skin but also from inhalation.

The reason that increasing numbers of reactions are being obtained must be attributed to more extensive testing. Instead of limiting ourselves to egg, milk and wheat in these young infants, we tested them with practically all proteins, including direct tests with substances derived from the immediate environment of the infant. Thus we discovered not only immediate offenders but also potential ones.

#### NATURAL PROGRESS

The discussion thus far has pertained to those infants under 1 year of age. In chart 1 is shown the age of onset for the entire series of 250 children in relation to the major allergic syndromes.

From our experience, it would seem that eczema starts earliest; very few, if any, new eczemas start after the sixth year. While asthma may have its onset at any time during childhood, very few cases appear to start in the first year; the largest number of asthmatic children date their first definite symptoms of dyspnea from the third to the fourth year. The story of hay fever is different; an occasional case may occur in early

23. Peck, S. M., and Salomon, Gustav: Eczema of Infancy and Childhood: I. Contacts as Etiologic Agents, with Particular Reference to Feathers, *Am. J. Dis. Child.* 46: 1308-1328 (Dec.) 1933.

24. Hopkins, J. G., and Kesten, B. M.: Allergic Eczema, *Am. J. Dis. Child.* 49: 1511-1530 (June) 1935.

25. Hill, L. W., and Sulzberger, M. B.: Evolution of Atopic Dermatitis, *Arch. Dermat. & Syph.* 32: 451-463 (Sept.) 1935.



The progress of the allergic conditions is interestingly delineated in charts 2 and 3. Here is shown the distribution of the allergic conditions among 250 children (chart 2) and among 315 adult allergic antecedents

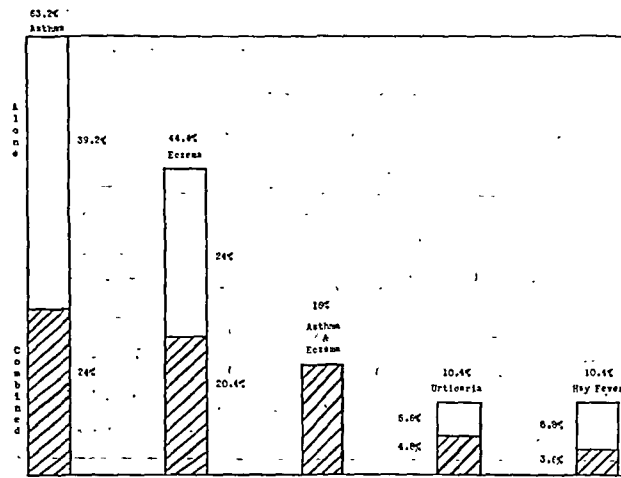


Chart 2.—Distribution of major syndromes among 250 allergic children either alone or combined with other syndromes.

(chart 3). The majority of children (63.2 per cent) suffer from asthma, as do the majority of adults (53 per cent). Among the children, however, only 39.2 per

sufferers among the adult antecedents is indicative of the trend. As I have already indicated, urticaria occurs sporadically, and from my own experience presents no significant trend in relation to age. Pure asthma remains the major form of allergy both in childhood and in the adult period. A rather interesting observation to be derived from our studies is that, in those cases which manifest more than one syndrome, asthma is generally present, and, in view of the preponderance of pure asthmatic cases it would appear that phylogenetically the human subject resembles the guinea pig in that the lung structure seems to be the predominantly reactive organ.

An analysis of the reactivities that allergic children manifested is drawn in chart 4. A larger number of food reactions occur in the youngest patients, although environmental substances begin to show reactions in the young and after the second year almost parallel food reaction. This picture is somewhat different from the observations of Stuart and Farnham,<sup>16</sup> who in discussing the acquisition and loss of hypersensitiveness in early life conclude that hypersensitiveness to food proteins tends to be present at birth and is gradually lost during childhood, whereas hypersensitiveness to inhalant proteins tends to be acquired during the middle period of the first decade and is more resistant to change. Bullen,<sup>28</sup> as well, has found that inhalants play a more prominent role in childhood than is generally thought.

TABLE 3.—Allergic Sensitivity in Relation to the Allergic Manifestations

	Non-sensitive	Foods	Inhalants-Contactants	Pollens	Foods and Inhalants-Contactants	Foods and Pollens	Foods, Inhalants-Contactants, Pollens	Inhalants-Contactants, Pollens
Eczema.....	14.3%	40.0%	5.7%	.....	31.4%	.....	8.6%	.....
Pure asthma.....	14.0%	11.5%	22.9%	0%	39.0%	3.0%	9.0%	0%
Asthma, eczema.....	5.7%	2.8%	5.6%	2.8%	48.5%	5.7%	26.1%	2.8%
Pure hay fever.....	.....	.....	.....	93.3%	.....	.....	14.2%	6.7%
Urticaria.....	42.9%	.....	14.3%	.....	28.6%	.....	.....	.....
Asthma, urticaria.....	33.3%	.....	33.3%	.....	33.3%	.....	33.3%	.....
Asthma, eczema, urticaria.....	.....	.....	.....	.....	66.7%	.....	50.0%	50.0%
Asthma, eczema, hay fever.....	.....	.....	.....	.....	.....	.....	75.0%	.....
Asthma, hay fever.....	.....	.....	25.0%	.....	.....	.....	.....	.....
Asthma, hay fever, urticaria.....	.....	.....	.....	.....	.....	.....	.....	.....
Asthma, eczema, urticaria, hay fever.....	.....	.....	.....	.....	.....	.....	.....	.....
Eczema, urticaria.....	Too few cases	.....	.....	.....	.....	.....	.....	.....

cent of those with asthma have this syndrome alone, whereas 24 per cent have it in combination with other syndromes—in the majority of instances with eczema. The largest number of infants under 1 year have eczema that antedates the onset of asthma, as has been brought out by Schloss,<sup>20</sup> Peshkin<sup>27</sup> and others. Practically all the food sensitive asthmatic patients gave an early history of eczema.

With the adult antecedents, it is interesting to note that the majority of asthmatic patients have asthma alone and that there were no cases of combined eczema and asthma. This (absence of eczema-asthma group) of course does not present a true state of affairs for I as well as others have seen adult patients with this combination of syndromes.

But it is the general trend of the progress of allergy with which I am concerned here, and comparing the two charts one sees that eczema, which is a dominant syndrome in childhood, particularly in infancy and earliest childhood, plays a lesser role as age advances. Hay fever, on the other hand, is of comparatively little significance in early childhood—particularly in the middle Atlantic states—and shows a definite rise as the age of the patient increases. The large number of hay fever

Peshkin<sup>29</sup> emphasizes this point, asserting that 98 per cent of his allergic children were sensitive to one or more substances of the inhalant group. This would

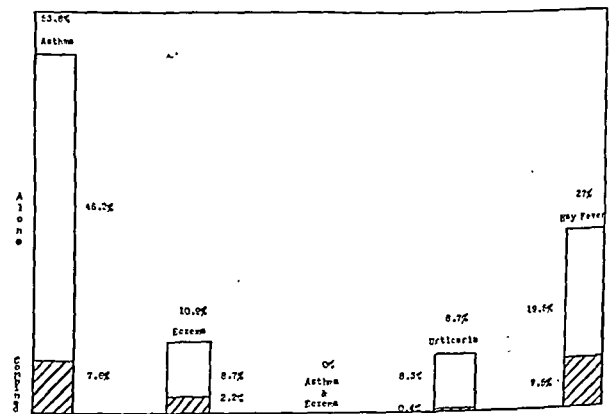


Chart 3.—Distribution of major syndromes among 315 adult antecedents.

indicate that a child exhibiting protein sensitization nearly always is sensitive to some inhalant. Peshkin states that this observation is somewhat at variance with

27. Peshkin, M. M.: Asthma in Children: II. The Incidence and Significance of Eczema, Urticaria and Angioneurotic Edema, *Am. J. Dis. Child.* 32:862-871 (Dec.) 1926.

28. Bullen, S. S.: Some Observations on the Natural History of Asthma in Childhood, *New York State J. Med.* 29:545 (May 1) 1929.  
29. Peshkin, M. M.: Asthma in Children: I. Etiology, *Am. J. Dis. Child.* 31:763-814 (June) 1926.

the earlier views that food sensitization was more commonly met than any other group. From Australia comes further supporting evidence by Barlow,<sup>30</sup> who states that environment has been rather underestimated as a factor in determining sensitization. In childhood,

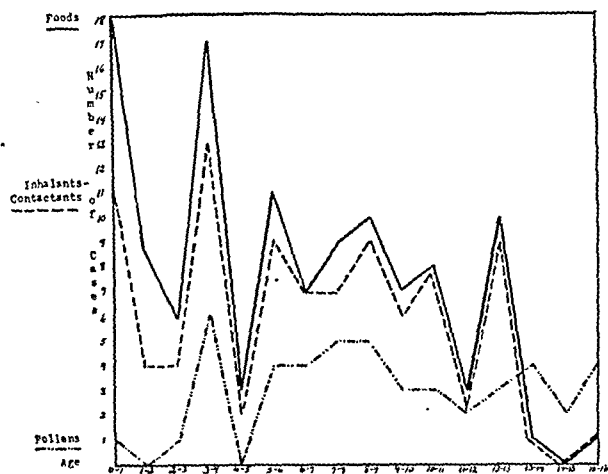


Chart 4.—Showing distribution of positive cutaneous reactions at the different ages: One hundred and nineteen patients reacted to foods, ninety-three to inhalants-contactants and forty-four to pollens.

the patient will often prove to be sensitive to food as well as to inhalant proteins, but only rarely are foods the main allergic factors.

In our series, pollens began to cause reactions at a later period than either foods or inhalants and contactants.

A further analysis of the distribution of these various reacting substances is presented in chart 5.

The relation that the allergenic sensitivity bears to the allergic manifestations is summarized in table 3. Among the patients with eczema, 40 per cent react to foods alone and 5.7 per cent to epidermals alone, the remainder reacting to a combination of foods, inhalants, contactants and pollens. With asthma, 11.5 per cent react to foods alone and a higher percentage (22.9) to inhalants. With the eczema-asthma group, 2.8 per cent react to foods alone, 5.6 per cent to inhalants alone and the overwhelming majority to various combinations. It is noteworthy that among patients with hay fever 93.3 per cent react to pollens alone, and 6.7 per cent to pollens and inhalants, which suggests that certain patients with hay fever, even in childhood, will not do well if tested and treated for pollen sensitivities alone.

These observations show clearly that, except for the youngest patients with eczema, who may be preponderantly sensitive to foods alone, the allergic patient must be suspected of being sensitive to multiple allergens in the various groups.

#### COMMENT

The varying criteria employed by different investigators make it difficult to compare our results with those of other students. For example, the fact that certain investigators limit themselves to the use of a few test substances whereas we have tested with all available proteins makes a comparison of results with respect to cutaneous reactivities meaningless.

Probably the greatest criticism that can be leveled against the present study, as well as others of a similar nature, is the fact that children of varying ages have

been grouped together and conclusions have been drawn as representative of childhood. To be really valid, an adequate number of cases at each age level should be studied. Each case should be studied with as many test materials as possible. Since such studies entail a vast amount of detail, and since the cases available to any single investigator are limited, it may be useful to collect material from several clinics. Conclusions drawn from data thus collected and properly collated would be of great value.

Failing such an ideal study it is useful at times to take stock of available observations, which may yield helpful suggestions.

That allergy can actually be manifested in the newborn and be present in the young infant under 1 year is of significance, for it must arouse in the physician a much keener appreciation for the need of early diagnosis. When one realizes that a large percentage of allergic adults first manifested symptoms in childhood, it is apparent that improperly diagnosed and untreated cases may persist for unnecessarily long periods.

That eczema is a forerunner of asthma in many instances is a fact that is known to all interested in this field and should become common knowledge to all physicians. More dermatologists today have an awakened interest in this subject and no longer regard these endermal manifestations as topical diseases but stress their constitutional nature (Hopkins and Kesten, Hill and Sulzberger, Peck and Salomon and others). It is true that infantile eczema must be treated locally,

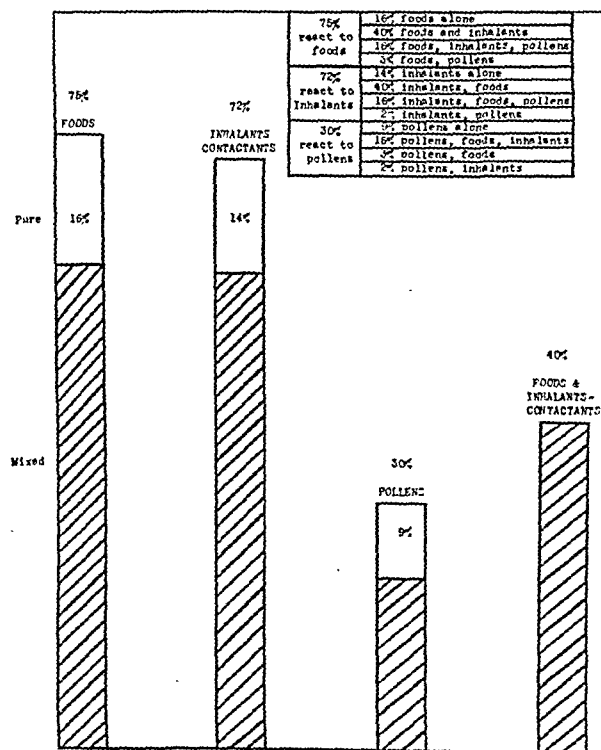


Chart 5.—Showing general distribution of positive cutaneous reactions.

but it is equally true that, unless the underlying reasons for the existence of the eczema are determined, recurrences and exacerbations must surely follow, and possibly the development of asthma.

One must also be alert to the early beginnings of respiratory allergy. In many instances, it is ushered in not by previous eczema but by recurrent episodes of

<sup>30</sup> Barlow, D. L.: Asthma in Children, *M. J. Australia* 1:4 (Jan. 1) 1938.

sneezing, lacrimation, rhinitis and attacks of coughing. The early episodes will perforce be treated symptomatically, but if these recur time and again the more serious allergic manifestations—asthma and hay fever—must be thought of.

Valid objections may be raised to the limited approach taken in the analysis of these cases, but I might state here that a discussion of all the other phases of the study of these cases relative to anamnestic data, eosinophil studies, the criteria employed in diagnosis, the psychogenic factors and the unreliability of the cutaneous test would have led us too far afield. These phases will be considered elsewhere. It will also be noted that I have made no attempt to discuss the intriguing question of prognosis for the reason that I was not concerned here with the progress of the individual case.

#### CONCLUSIONS

No dogmatic conclusions can be drawn with respect to the onset and progress of allergic syndromes in childhood. This is due to the fact that our knowledge of the underlying mechanism of allergy is still far from complete.

It is apparent that allergy may start at an extremely early age. The newborn period is signally free, with the rare exception of an occasional instance of passive sensitization acquired in utero.

Eczema is the prevailing allergic syndrome in infants under 1 year of age, and foods are the prevailing reacting substance. Though food sensitivities were found in 100 per cent of our patients under 1 year of age, they are nevertheless not always the sole cause of the allergic syndrome. The allergic eczemas in many instances (59 per cent) are shown to be due largely to contact with environmental substances to which these same infants react.

Infants who react to egg and other food proteins which they have never ingested have most probably been actively sensitized in utero. The early allergic manifestations may be invoked by a passage of these substances through the breast milk in infants previously sensitized in utero. On the other hand, such potential sensitivities may cause allergic reactions when these foods are eventually added to the diet in the latter part of the first year.

The age of onset of eczema is considerably earlier than that of asthma and, in many instances, it is the forerunner of asthma.

After early infancy, asthma becomes the prevailing allergic syndrome, and wherever there is a multiplicity of syndromes asthma is generally one of the complicating conditions. Asthma was also the dominant form in the allergic antecedents of the children studied. It appears, therefore, that the lung structure is phylogenetically predisposed to sensitization in the human species as it is in the guinea pig.

Hay fever is not of great significance in early infancy in the middle Atlantic states. It comes to the fore in the latter part of the first decade and becomes a prominent syndrome in the second decade of life.

Urticaria at all times remains sporadic and shows no particular age alinement.

Though food sensitivities play a very important role in the allergy of childhood, inhalants and contactants play an equally important one. Throughout infancy and childhood reactions to foods and inhalants and contactants run a parallel course. There are many infants and children who react to pollens who do not suffer

from hay fever. The pollens may be contributing factors in the eczema or asthma, or they may indicate potential sensitivities which eventually cause the onset of hay fever.

The preponderance of multiple reactivities would suggest that specific therapeutic measures may fail if all the offending factors are not taken into account.

The onset of allergy can in a measure be prevented through control of the diet of the pregnant woman and of the young infant. Cognizance of the important role that environmental inhalant substances play in earliest infancy too must lead to prophylactic measures.

The progress of allergy can be interrupted by early diagnosis of the interrelated syndromes and reduction of contact with inciting substances.

It is true that in the present state of our knowledge it is difficult actively to engage the interest of the physician who is unprepared by training and equipment in this subject, which appears to be complicated by so many factors and which from many reports seems to yield but few satisfactory results.

The time must soon arrive, however, when the salient facts, gleaned from the maze of work that is being carried on, will be separated from the chaff and formulated into broad principles that can be more readily applied in general everyday practice.

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#### ABSTRACT OF DISCUSSION

DR. MILTON B. COHEN, Cleveland: It is interesting to me, an allergist interested in pediatrics, to hear a paper by Dr. Ratner, a pediatrician interested in allergy, and to find that there is no essential disagreement in our points of view. This arises, I believe, from the fact that as clinicians study any disease, no matter what discipline they bring to the study originally, they ultimately arrive at certain general conclusions which are in agreement. This paper calls attention to the fact that the pediatrician is the one who is going to see the earliest manifestations of allergy and going to see the child at a time when certain destructive processes produced by long-standing disease may be prevented. It is very important that one think of allergy not as asthma or hay fever or allergic rhinitis or urticaria, but as a clinical condition which may manifest itself anywhere in the child economy and that one follow it wherever it goes and treat it accordingly. Therefore, it doesn't make a great deal of difference whether in your practice the statistics vary slightly from Dr. Ratner's or whether in my practice they do. The important thing is that this condition should be recognized early. It can be recognized early and, if it is managed early, many of the changes which occur in adult life may be avoided.

DR. TELL NELSON, Evanston, Ill.: I am in accord with what Dr. Ratner has pointed out. That allergy is common in infancy and childhood cannot be discounted. But, unfortunately, it is often minimized and frequently overlooked. Dr. Ratner stated that between 50 and 60 per cent of adults date their allergy from early childhood. In a series compiled some years ago, I found that in 66 per cent of all my cases the allergic symptoms had started before 20 years of age. It is interesting that in the first decade twice as many males develop allergic manifestations as females. In this study I took into consideration eczema, asthma and hay fever, including in hay fever the hypersensitive rhinitis type of manifestation. What the difference in sex means, I am not ready to state. I was happy to hear Dr. Ratner stress the inhalant factors in addition to the foods in infants and children. I find inhalants as important in early infancy as foods. Dr. Ratner also mentioned the finding of hay fever, of pollen sensitivity, as starting early in life and being very gradual, beginning to manifest itself in a fairly good proportion along about 6 years of age. He stated that this was probably due to the fact that their cases may differ somewhat because of location. In the Middle

West I find a goodly proportion of my patients definitely pollen sensitive quite early in life. I can't give exact figures, but in my own practice and in the clinics a large percentage of children manifest definite hay fever symptoms at 2 and 3 years of age. It is only by careful study of children who manifest frank allergic symptoms and the recognition of those children who manifest early stigmas of the allergic constitution that it will be possible to manage this type of individual better and avoid the trouble which will appear later in life.

## RENAL TUBERCULOSIS: PROGNOSIS FOLLOWING NEPHRECTOMY

BASED ON PREOPERATIVE OBSERVATIONS IN THE  
"GOOD" KIDNEY

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The indications for nephrectomy in the presence of renal tuberculosis are commonly discussed. Opinion on this subject is unsettled, partly because of lack of agreement concerning the pathogenesis of the disease. One group of investigators, following Medlar's teaching, feels that renal tuberculosis always begins with bilateral involvement, while another group maintains that it begins in most cases as a unilateral infection. This argument has academic interest, but the patient desires only to be relieved of his symptoms and to have his life prolonged.

Generally speaking, four clinical methods can be employed to investigate a kidney in the presence of this disease: (1) urography, (2) determination of the amount of pus present in the specimen of urine obtained by ureteral catheterization, (3) inoculation of guinea pigs with the specimen of urine obtained by ureteral catheterization, and (4) an attempt to demonstrate the bacilli of tuberculosis in stained smears of the specimen of urine obtained by ureteral catheterization. Past experience has taught that none of these tests are infallible; therefore it may be said that in renal tuberculosis it is impossible to prove clinically that one kidney is free of infection. Nevertheless, all the tests are valuable and the question today is how many of these tests should be employed and the finding of what manifestations relative to the so-called uninvolved kidney should be insisted on before subjecting the patient to removal of the involved kidney. It would seem that the most practical approach to this problem would be to study the postoperative results in a large group of cases of renal tuberculosis in which nephrectomy had been performed. By grouping these cases according to the method of investigation and according to the observations obtained in relation to the so-called uninvolved kidney, a comparative analysis of the operative results should be possible and should help to solve this problem. We have attempted to carry out this plan of study in the analysis of a series of cases and trust that further analysis of the results will be of some practical value. For brevity we shall refer in this paper to the diseased kidney that was removed at operation as the "bad"

kidney, while the so-called uninvolved kidney will be spoken of as the "good" kidney. Also for brevity it will be said herein that "guinea pigs were positive" or "negative" rather than that "the result of inoculation of guinea pigs was positive" or "negative."

We have studied the records of 1,131 consecutive patients on whom nephrectomy was performed for renal tuberculosis at the Mayo Clinic between the years 1912 and 1932 inclusive. The results in these cases have been studied from the standpoint of the observations obtained in the clinical investigation of the good kidney prior to operation. No attention has been paid to the condition of the bad kidney which was removed or to the type of surgical technic employed. Pathologic conditions outside the urinary tract, both tuberculous and nontuberculous, have been disregarded as they are probably evenly distributed among the artificial groups we have made for comparison and would therefore not seriously affect the analysis. No patients were studied who were operated on after 1932, in order that all cases might be studied from the standpoint of at least five year survival. Of the 1,131 patients, 453 were known to be dead. To the remaining 678 patients letters of inquiry were sent, answers to which were received in more than 70 per cent of cases. In many of the cases in which replies were not received, as well as in many of those in which the patients were known to be dead, the records contained previous correspondence, including replies to questionnaires of previous years, which supplied considerable information. In our letter of inquiry we asked the patient if, and to what extent, his vesical trouble had improved since his operation, and further we requested him to state the number of times he found it necessary to void both day and night and the amount of pain or burning that accompanied urination. Inquiry also was made as to the state of his general health. From the information obtained, the following classification of results was formulated:

1. Patients dead. Information on this group also included the date of death.
2. Patients cured. Only those patients who were entirely free of all vesical symptoms were included in this group.
3. Patients improved. These were patients whose vesical symptoms had improved since operation but vesical symptoms of some kind, even though slight, still persisted. The group included patients whose bladders were contracted and whose frequency of urination persisted in spite of microscopically negative urine. It also probably included a generous number of patients in examination of whom, if cystoscopy was done, pathologic change would not be found.
4. Patients unimproved. This group included those whose vesical symptoms were not improved or became worse.
5. Condition unknown. These were patients who at the time of writing this report we knew were still alive but we were unable to ascertain their condition.

Regarding the patients who were dead, no attempt was made to study the cause of death, as such reports are so unreliable in most cases as to be practically valueless from a statistical standpoint. Although we are sure that a large number of these patients died from causes unrelated to their renal tuberculosis, we feel that they were well enough distributed throughout the various groups in this study as not seriously to affect the comparative results. In other reliable reports in the literature are estimates of the mortality that may be expected from tuberculosis elsewhere than in the urinary tract, so that this phase was not studied in our

• From the Section on Urology, the Mayo Clinic.  
Read before the Section on Urology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.

series of cases. All percentages recorded in the accompanying tables were based on the number of traced patients as denoted in each table.

A word should be said about the terms "cured" and "improved." It would seem that, if a patient is in good health from ten to twenty years after operation but still complains of moderate frequency of urination, the assumption would be justified that the tuberculous process had been eradicated and the patient probably cured. This interpretation has been used in most statistical papers on renal tuberculosis. We have preferred, however, to list such patients as "improved" only, reserving the term "cured" for complete absence of symptoms referable to the bladder. For this reason, in a comparison of our tables with those of some other authors, a total of our cured and improved patients would more nearly correspond to "patients well" in their reports.

There seems to be little if any preference of the disease for either side, as the right kidney was removed in 602 cases and the left in 529 cases.

#### AGE

The average age of the patients operated on varied little from year to year during the twenty years of the study. We felt that it would be of interest to determine whether there was any great variation in postoperative results among patients of the various age groups. Table 1 indicates that there was essentially no difference. Although results obtained with patients of the second and seventh decades differed somewhat from the results obtained with patients of the other decades, it must be borne in mind that the patients of these two decades who were traced were too few to yield accurate percentages. The youngest patient operated on was 8 years of age and the oldest 71 years of age.

TABLE 1.—Comparison of Five Year Results on the Basis of Age by Decades in 1,131 Cases of Renal Tuberculosis in Which Nephrectomy Was Performed, 1912 to 1932 Inclusive

Decade of Life	Total Patients	Traced Patients	Patients Living										
			Patients Dead		Cured		Improved		Unimproved		Condition Unknown		
			Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced	
0-9	1	1	..	....	1	100							
10-19	47	41	14	34.1	11	26.8	9	30.0	7	17.1	0	0	
20-29	291	265	62	23.4	108	40.7	57	21.5	27	10.2	11	4.2	
30-39	417	373	88	23.6	159	42.6	66	17.7	33	8.9	27	7.2	
40-49	246	227	54	23.8	91	40.1	58	25.5	17	7.5	7	3.1	
50-59	110	98	28	28.6	36	36.7	16	16.3	12	12.2	6	6.2	
60-69	18	16	10	62.4	4	25.0	1	6.3	1	6.3	0	0	
70-79	1	1	..	....	..	....	1	100					

TABLE 2.—Comparison of Results with Male and Female Patients in 1,131 Cases of Renal Tuberculosis in Which Nephrectomy Was Performed, 1912 to 1932 Inclusive

Years After Operation	Total Patients		Traced Patients		Patients Dead, per Cent of Traced		Patients Living, per Cent of Traced							
							Cured		Improved		Unimproved		Condition Unknown	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
5	724	407	658	358	30.5	15.1	33.6	53.7	18.4	23.2	12.0	4.7	5.5	3.3
10	595	336	494	259	47.4	26.2	29.0	51.0	13.0	16.6	4.8	2.0	5.8	4.2
15	426	240	335	178	59.1	36.0	26.8	47.2	7.2	13.2	3.6	0	3.3	1.6
20	227	106	175	76	66.3	44.7	25.7	44.7	4.6	7.9	1.1	0	2.3	2.7

As has been stated previously, the primary object of this study was to learn the results of nephrectomy from the standpoint of the preoperative observations obtained in the investigation of the good kidney. We shall include also, however, regarding this rather large group of cases, a few general statistics that should be of especial interest to the student of this subject.

#### INCIDENCE

The number of cases in which nephrectomy has been performed at the clinic each year since 1912, for renal tuberculosis, indicates a definite reduction in the incidence of this disease. For instance, in the six years 1920 to 1925 inclusive an average of fifty-nine patients with renal tuberculosis were subjected to nephrectomy yearly, whereas in the six years from 1932 to 1937 inclusive the yearly average was only twenty-six. These figures are particularly significant when one considers that the average number of patients admitted to the clinic yearly from 1932 to 1937 inclusive was 9.3 per cent higher than in the six years 1920 to 1925 inclusive.

#### SEX

The disease affected almost twice as many males as females. Nephrectomy was performed on 724 males and on only 407 females (table 2). The most striking information obtained from this table, however, is the difference in the clinical results following operation in persons of the two sexes. That the disease is far more serious to the male is shown by the fact that in the study of ten year survivals almost twice as many males as females were dead, whereas the incidence of cure among females was strikingly higher than it was among males. The reason for these differences is not obvious but the rather common occurrence of associated genital tuberculosis in the male may be a factor.

#### POSTOPERATIVE RESULTS FROM THE STANDPOINT OF THE "GOOD KIDNEY"

In this part of the paper are reported matters pertaining to the primary purpose of the study, namely postoperative results from the points of view of the method of investigation applied to, and the clinical results

obtained from, the good kidney prior to operation. The patients were divided into four main groups as follows: Group 1, patients whose good kidney was not catheterized prior to operation. Group 2, patients whose good kidney was catheterized prior to operation, and microscopic examination of the centrifuged ureteral specimen of urine revealed either no pus cells or not more than three pus cells per high power field. Group 3, patients whose good kidney was catheterized prior to operation and microscopic examination of the ureteral specimen of urine revealed from three to ten pus cells per high power field. Group 4, patients whose good kidney was catheterized prior to operation and microscopic examination of the ureteral specimen of urine revealed more than ten pus cells per high power field. We have

the good kidney was carried out in 369 cases, or 76.4 per cent of the 483 cases in which operation was performed, whereas between 1920 and 1932 it was carried out in 604 cases, or 93.2 per cent of the 648 cases in which operation was performed. Inability to catheterize the ureter on the good side in the presence of extremely irritable or contracted bladders is another common reason for omission of catheterization.

Table 3 discloses that the mortality rate both five and ten years after operation was much greater in group 1 than it was in group 2 (the group in which the urine was microscopically negative). On the other hand, the mortality rate was about equal to that of groups 3 and 4. From the standpoint of patients cured the difference was not so striking, but there was still

TABLE 3.—Comparison of Results Based on the Number of Pus Cells Found on Microscopic Examination of the Centrifuged Urine Obtained by Ureteral Catheterization from the "Good" Kidney in 1,131 Cases of Renal Tuberculosis in Which Nephrectomy Was Performed, 1912 to 1932 Inclusive

Years After Operation	Group*	Total Patients	Traced Patients	Patients Living									
				Patients Dead		Cured		Improved		Unimproved		Condition Unknown	
				Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced
5	1	161	145	50	34.5	49	33.8	24	16.6	14	9.6	8	5.5
	2	802	713	146	20.3	312	43.5	156	21.7	61	8.5	43	6.3
	3	121	108	47	43.5	31	28.8	13	12.0	11	10.2	6	5.5
	4	47	45	15	33.4	9	20.0	11	24.4	8	17.8	2	4.4
10	1	145	121	62	51.2	37	30.6	12	9.9	4	3.3	6	5.0
	2	649	522	182	34.8	207	39.7	87	16.7	22	4.2	24	4.6
	3	103	87	45	51.7	24	27.6	10	11.5	6	6.9	2	2.3
	4	34	25	14	56.0	5	20.0	6	24.0	0	0	0	0

\* Group 1, "good" kidney not catheterized. Group 2, "good" kidney catheterized; microscopic examination of urine specimen disclosed from 0 to 3 leukocytes per high power field. Group 3, "good" kidney catheterized; microscopic examination of urine specimen disclosed from 3 to 10 leukocytes per high power field. Group 4, "good" kidney catheterized; microscopic examination of urine specimen disclosed more than 10 leukocytes per high power field.

TABLE 4.—Summary of Results in 1,131 Cases of Renal Tuberculosis in Which Nephrectomy Was Performed, 1912 to 1932 Inclusive

Years After Operation	Total Patients	Traced Patients	Patients Living									
			Patients Dead		Cured		Improved		Unimproved		Condition Unknown	
			Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced
5	1,131	1,016	225	25.1	413	40.7	204	20.6	96	9.5	48	4.7
10	931	753	302	40.1	275	36.5	107	14.2	29	3.9	40	5.3
15	666	513	262	51.1	174	33.9	51	9.9	12	2.3	14	2.8
20	333	251	150	59.7	79	31.5	14	5.6	2	0.8	6	2.4

compared these four groups of patients in table 3; no attention was paid to inoculation of guinea pigs or to acid-fast staining. The patients are compared as to postoperative results both five and ten years following operation. In group 1 there were 161 patients. The question may be asked as to why the good kidneys in these cases were not catheterized. The majority of cases in this group are those in which diagnosis was made and operation performed between 1912 and 1920, when cystoscopic instruments and technic had not reached the refinement that has been attained in the last twenty years. In many of these cases cystoscopic examination revealed thick pus exuding from the ureteral orifice on one side and clear urine spurting from the ureteral orifice on the other side; nephrectomy was carried out on the basis of this information only. For instance, in the series of cases in which operation was performed between 1912 and 1920, catheterization of

a much larger percentage of cures in group 2, as would be expected. There was a much higher percentage of cures in group 1 than in group 4, which can be explained by the fact that all the good kidneys in group 4 contained considerable amounts of pus, whereas in group 1 a large percentage of kidneys were no doubt secreting microscopically negative urine. One important point must not be overlooked, and that is that 20 per cent of the patients in group 4 (the group in which more than ten cells per high power field were found in the ureteral specimen of urine) were cured ten years after operation. Although the number of patients traced in this group was so small that the percentage had little statistical value, it nevertheless is significant and must be taken into consideration. This will be considered more fully later. When the results in these four groups are compared with the results obtained in the series as a whole, regardless of method of diagnosis



(table 4), the results in group 2 are seen to be considerably better than the average for the entire series.

In an effort to evaluate the importance of investigating the good kidney by inoculation of guinea pigs and acid-fast staining of the urine obtained by ureteral catheterization, group 2, 3 and 4 each was broken down into divisions A, B and C. Division A indicates that guinea pigs were not inoculated and that positive acid-fast stains were not obtained. Division B indicates that guinea pigs were inoculated but that the results were negative and that positive acid-fast stains were not obtained. Division C indicates that either inoculation of guinea pigs or acid-fast stains, or both, were positive. The results in these various divisions of cases are compared in tables 5, 6 and 7. We speak only of acid-fast

value as far as percentages are concerned because the number of cases in each of these divisions was small. However, the tables do present points of interest. The most striking observation is the exceedingly high mortality in division C of both groups. No patients in group 4 C were cured in either five or ten years, whereas two patients in group 3 C were reported cured after ten years. Also seven patients in group 4 A were reported cured after five years and four after ten years, while less than this in group 4 B were cured.

#### UROGRAPHY

Before any deductions are drawn from the foregoing data a word should be said concerning the evaluation of urograms in this condition. As the cases in this

TABLE 5.—Analysis of Results in Group 2, Based on Inoculation of Guinea Pigs and Demonstration of Bacilli of Tuberculosis by Stain of the Urine Obtained from the "Good" Kidney by Ureteral Catheterization

Years After Operation	Group*	Total Patients	Traced Patients	Patients Dead		Patients Living							
						Cured		Improved		Unimproved		Condition Unknown	
				Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced
5	2 A	513	454	95	20.9	195	43.0	96	21.1	36	7.9	32	7.1
	2 B	229	209	28	13.3	150	50.3	52	24.9	18	8.6	6	2.9
	2 C	60	55	23	41.8	12	21.8	8	14.6	7	12.7	5	9.1
10	2 A	476	379	131	34.6	150	39.6	61	16.1	16	4.2	21	5.5
	2 B	136	113	31	27.4	61	45.1	23	20.4	6	5.3	2	1.8
	2 C	37	30	20	66.7	6	20.0	3	10.0	0	0	1	3.3

\* Group 2, "good" kidney catheterized; microscopic examination of urine specimen contained from 0 to 3 leukocytes per high power field. A, no guinea pig inoculated, no positive acid-fast stains obtained. B, negative guinea pig, no positive acid-fast stains obtained. C, positive guinea pig or positive acid-fast stain obtained, or both positive.

TABLE 6.—Analysis of Results in Group 3, Based on Inoculation of Guinea Pigs and Demonstration of Bacilli of Tuberculosis by Stain of the Urine Obtained from the "Good" Kidney by Ureteral Catheterization

Years After Operation	Group*	Total Patients	Traced Patients	Patients Dead		Patients Living							
						Cured		Improved		Unimproved		Condition Unknown	
				Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced
5	3 A	89	77	33	42.9	22	28.5	11	14.3	5	6.5	6	7.8
	3 B	17	16	6	37.6	7	43.8	1	6.3	2	1.3	0	0
	3 C	15	15	8	53.3	2	13.3	1	6.7	4	26.7	0	0
10	3 A	85	69	37	53.6	18	26.1	9	13.0	3	4.3	2	3.0
	3 B	8	8	2	25.3	4	50.0	1	12.5	1	12.5	0	0
	3 C	10	10	6	60.0	2	20.0	0	0	2	20.0	0	0

\* Group 3, "good" kidney catheterized; microscopic examination of urine specimen disclosed from 3 to 10 leukocytes per high power field. A, no guinea pig inoculated, no positive acid-fast stains obtained. B, negative guinea pig, no positive acid-fast stains obtained. C, positive guinea pig or positive acid-fast stain, or both positive.

stains that were positive, because we feel that a negative stain of a catheterized ureteral specimen of urine is of little significance. In table 5 the cases in group 2 (with microscopically negative urine from the good kidney) are considered from the point of view of inoculation of animals and of acid-fast staining. The striking observation is the extremely high mortality in the division in which either positive guinea pigs or positive stains, or both, were obtained (division C) as contrasted with the division in which inoculation of guinea pigs proved negative and positive acid-fast stains were not obtained (division B). The percentage of cures in division B is also markedly higher than that in division C. The percentage in division A (guinea pigs not inoculated and positive acid-fast stains not obtained), as would be expected, falls between those of the other two divisions.

Tables 6 and 7, comparing group 3, divisions A, B, C and group 4, divisions A, B, C are of no statistical

series were not studied later than 1932, few excretory urograms were made. Nearly all the urograms were retrograde pyelograms. In the entire series of cases these pyelograms were made of the good kidney in forty-five cases. Of these, thirty-eight were considered normal. Thirty-five of the patients who gave normal pyelograms were traced five years, at which time 30 per cent were dead and 40 per cent were reported as cured. These results are about the same as for the entire series of cases (table 4). There were, however, too few pyelograms to warrant any conclusion being drawn from their study.

#### COMMENT

What, then, can be deduced from the information derived from study of the comparative results in these various groups of cases, and in what way can it assist in the diagnosis and plan of treatment in renal tuber-

culosis? In the first place, to make a fairly accurate prognosis, catheterization of the good kidney, to determine the amount of pus being secreted, is imperative. A negative urine in such a case leads to a favorable prognosis and our statistical data indicate that the patient may expect approximately 43.5 per cent chance of a five year cure, a 65.2 per cent chance of being cured or improved in that period and only a 20.3 per cent chance of death within five years. If, in addition to this, inoculation of a guinea pig gives a negative result and a positive acid-fast stain is not obtained, his chance of dying within five years will drop to 13.3 per cent, his chance of a five year cure will be increased to 50.3 per cent, and his chance of being either cured or improved will increase to 75.2 per cent. On the other hand, if the guinea pig is positive, the patient's chance of dying within five years increases to 41.8 per cent and his chance of a five year cure drops to 21.8 per cent. These figures are dramatic and demonstrate that the results differ greatly in cases in which the urine from the good kidney is negative, depending on whether the guinea pig is positive or negative.

The question then arises Should a positive guinea pig corresponding to the good kidney, in spite of

guinea pig or the stain is positive, the prognosis is poor and it is questionable if operation is warranted. In such cases, no doubt, fairly advanced bilateral renal tuberculosis is present and the possibility of clinical improvement of the better of the two kidneys, following operation, certainly is questionable. If there is a small amount of pus, if guinea pigs and stains are negative, and if the excretory urogram is normal, the prognosis seems to be reasonably good and possibly surgical measures are worth the trial. This is especially true if there are not more than ten or fifteen pus cells per high power microscopic field in the centrifuged ureteral specimen of urine.

One might well ask whether this study sheds any light on the old arguments whether renal tuberculosis is essentially bilateral and whether healing ever takes place in renal tuberculosis. Comparing the groups and divisions (2 C, 3 C and 4 C), it is seen that in group 2 C there is a considerably higher percentage of five and ten year cures, in spite of the positive guinea pig. There are fewer in group 3 C but still a fair number, whereas in group 4 C there are no five or ten year cures. Group 4 C, including as it does the cases in which guinea pigs or stains were positive and a considerable amount of

TABLE 7.—Analysis of Results in Group 4, Based on Inoculation of Guinea Pigs and Demonstration of Bacilli of Tuberculosis by Stain of the Urine Obtained from the "Good" Kidney by Ureteral Catheterization

Years After Operation	Group*	Total Patients	Traced Patients	Patients Dead		Patients Living							
						Cured		Improved		Unimproved		Condition Unknown	
				Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced	Number	Per Cent of Traced
5	4 A	24	23	4	17.4	7	30.4	7	30.4	3	13.1	2	8.7
	4 B	11	10	3	30.0	2	20.0	3	30.0	2	20.0	0	0
	4 C	12	12	8	66.7	0	0	1	8.3	3	25.0	0	0
10	4 A	20	14	6	42.8	4	28.6	4	28.6	0	0	0	0
	4 B	8	5	2	40.0	1	20.0	2	40.0	0	0	0	0
	4 C	6	6	6	100.0	0	0	0	0	0	0	0	0

\* Group 4, "good" kidney catheterized; microscopic examination of urine specimen disclosed more than 10 leukocytes per high power field. A, no guinea pig inoculated, no positive acid-fast stains obtained. B, negative guinea pig, no positive acid-fast stains obtained. C, positive guinea pig or positive acid-fast stains, or both positive.

absence of pus in the urine, be considered a contraindication to surgical operation? It must not be forgotten that 21.8 per cent of such patients were cured, that a total of 36.4 per cent were either cured or improved at the end of five years, and that 30 per cent were either cured or improved at the end of ten years. Certainly almost any one who had the disease would be willing to submit to operation if given a 30 to 36.4 per cent chance of improvement for from five to ten years. If other factors do not constitute contraindications to surgical operation, and if the excretory urogram of the good kidney is within normal limits, it seems to us that a positive guinea pig should by no means be considered a contraindication to surgical measures, although it would considerably alter the prognosis. The common procedure, therefore, of performing nephrectomy in such cases, without awaiting the report of inoculation of animals, would appear to be justified.

When pus is found in the catheterized specimen of urine from the good kidney, the problem is radically altered. Because of the small number of such cases in our series it is difficult to make as far-reaching statements as have been made concerning the cases in which the urine was microscopically negative. However, tables 6 and 7 suggest that if more than three pus cells per high power microscopic field are found and the

pus was present, no doubt represents advanced lesions which probably are those which Thomas would classify as destructive lesions. In these cases progress would be expected to be poor. The cured patients in group 2 C and group 3 C, however, are not so easily explained. No doubt the positive finding in some cases is owing to reflux of vesical urine up the ureter or is attributable to the catheter, as it is passed through the bladder, picking up bacteria and pus. However, certainly some of these must have been bona fide cases of bilateral renal tuberculosis. That the lesion in the kidney became quiescent or clinically healed seems probable, although of course a conclusion cannot be reached unless the kidney is examined microscopically.

Although what has been written here does not settle the academic argument, it does clarify the practical phase of the subject, which is the only one in which the patient is interested. We believe that on a basis of these figures, which are drawn from a relatively large group of cases, it should be possible for the physician to give his patient a fairly accurate prognosis after complete study of the good kidney, including urography. The estimate, of course, must be tempered by consideration of the general condition of the patient, the presence or absence of associated disease (whether tuberculous or otherwise) and the approximate length of time the disease has been in progress.

## ABSTRACT OF DISCUSSION

DR. JOHN R. HAND, Portland, Ore.: The authors should be commended for their effort to crystallize our knowledge of the basic facts on which the surgical indications for nephrectomy and the prognosis are based. They have suggested that the study should include urograms, analysis of the degree of pyuria, inoculation of guinea pigs and staining the specimens obtained by ureteral catheterization of the good kidney to detect acid-fast organisms. I would add determination of the comparative functional capacity of the good kidney. This would probably be of greatest value when the prognosis was poor, that is, when pyuria was present. The authors' analysis allows one to visualize four important pictures: 1. That of a kidney not excreting pus or acid-fast bacilli. The patient with this type may expect a 50 per cent chance of cure, a 75 per cent chance of improvement and a 13 per cent chance of death within five years. 2. That of a kidney not excreting pus but excreting acid-fast bacilli. There is an area of caseous necrosis in which acid-fast organisms are escaping through the tubules but in which a pyogenic reaction has not yet occurred at the papilla. The patient stands a 21 per cent chance of cure, a 36 per cent chance of improvement and a 41 per cent chance of death within five years. (These two pictures make one realize that the acid-fast bacilli obtained in the specimen from the good kidney are in most instances not due to contamination.) 3. That of "a good kidney" with a normal urogram. The patient stands a 40 per cent chance of cure and a 30 per cent chance of death within five years. This picture emphasizes that even when the urogram is normal, acid-fast organisms may be coming from the kidney. 4. That of a kidney in which caseous necrosis, ulceration and a pyogenic reaction are taking place at the renal papilla, allowing the excretion of pus. Whether or not this pyuria is accompanied by excretion of acid-fast bacilli, the prognosis is poor. This paper reflects credit not only on Drs. Emmett and Kibler but on the teamwork and skill of the clinicians and surgeons who made their exceptional results possible.

DR. FREDERICK LIEBERTHAL, Chicago: It is natural to assume that an early lesion in the good kidney may heal after the removal of the bad kidney. Instances of such healing have been reported in the literature. The authors do not say how long they carried on their follow-ups, and hence the accuracy of their statistics is to be questioned. When one considers that tuberculosis may run its course for decades or even a lifetime, that long remissions may occur and that renal tuberculosis affects mainly persons between 20 and 40, in other words persons who would under normal circumstances have a long life expectancy, it immediately becomes clear that follow-ups of five, ten or even twenty years are imperative if accurate conclusions are to be drawn as to the ultimate fate of the patient. I believe therefore that in this regard Drs. Emmett and Kibler have struck the keynote of the problem, for I am convinced that many of the errors in the literature concerning renal tuberculosis are due to the fact that the follow-ups were too short. In this series the turning point seemed to come in those cases in which the separated urine from the good kidney contained fewer than 3 pus cells per high power field. The question naturally arises as to the extent of the lesions in these cases. A cell count of lower than 10 per field when there is good renal function and the excretory urogram is normal denotes that the renal lesion is limited to a solitary caseous ulcer on one renal papilla which scarcely covers the summit of the papilla. The fact that such a minute solitary lesion in the good kidney reduces the chances of a five year improvement or cure after removal of the bad kidney to only 21 per cent is worthy of consideration. Today there is a great tendency to treat frankly unilateral renal tuberculosis conservatively. I believe that this study offers a prophecy of the disastrous results which may be expected when ten and twenty year follow-ups become available for such treatment.

DR. J. C. NEGLEY, Los Angeles: My experience includes seventeen years of work in a tuberculosis sanatorium and eighteen years of work in a large clinic. I realized after a number of years that when the so-called good kidney was not catheterized bilateral renal tuberculosis was undiagnosed in many cases. The close correlation between the development of renal tuberculosis in the remaining kidney and bilateral renal tuberculosis diagnosed at the first examination is worthy of

note. In a series of cases which I reported four years ago, tuberculosis developed in the remaining kidney in about 4.5 per cent of all the cases in which operation was performed. In about 10 per cent bilateral renal tuberculosis was observed at the first examination. In the Urologic Clinic renal tuberculosis in the remaining kidney developed in 12.5 per cent of the cases and bilateral involvement was present when the diagnosis was first made. I offer a very radical procedure, for which I have been criticized. For the past seventeen years at the Olive View Sanitarium it has been the custom to take two sets of pyelograms every time a patient of mine is examined. That is, I make bilateral pyelograms with catheters at or near the renal pelvis and immediately afterward a bilateral set with the catheters at or near the level of the bladder. In seventeen years I have had no disastrous results. No patient has died. I have had no more reaction than if I had catheterized but one side, and the fear, always present, of setting up acute miliary tuberculosis through the pyelovenous back flow has never materialized. In the authors' paper a great deal of emphasis has been placed on not catheterizing the good kidney. If the good kidney is not catheterized, how does one know whether it is a good kidney or a bad one? The cases reported are similar to those observed at a large urologic clinic. The patient comes because he has symptoms, generally directed to one side. One kidney is catheterized and removed, and then the patient leaves. Constant contact is not possible. In the tuberculosis sanatorium, however, patients are under control at all times. Repeated examinations are performed as they show symptoms or as their bladder urine shows pathologic changes. In a number of cases bilateral renal tuberculosis is diagnosed. Despite the fact that the procedure is radical, I do not consider any case of renal tuberculosis studied completely until two sets of bilateral pyelograms such as I have described have been made, plus a test for pus cells, smears and inoculation of guinea pigs.

DR. WILLIAM P. HERBST, Washington, D. C.: There are several interesting phases of this tuberculosis problem. One should not forget that whether the patient gets well or not depends on his resistance and that renal tuberculosis is not a local but a constitutional disease. Gilbert Thomas has emphasized this fact repeatedly. All patients who have had a nephrectomy for renal tuberculosis should be treated with sanatorium care for a year in order to give their generalized tuberculous process a chance to heal and to improve the end results from the standpoint of lowering the incidence of involvement of the remaining kidney. Natural resistance to tuberculous infection varies markedly. Not infrequently one sees a patient who refuses surgical intervention carrying on for ten years or more and yet having extensive, active bilateral involvement. Such observations justify conservative handling in the early stages and reemphasize the necessity of complete sanatorium rest after nephrectomy whenever it is economically possible.

DR. JOHN M. KIBLER, Rochester, Minn.: Dr. Negley asked how we could be sure that one kidney was good. The terms good and bad were used only in a relative manner and were defined rather arbitrarily at the beginning of the paper. By "bad" kidney we mean the more involved of the two kidneys; by "good" kidney we mean the uninvolved kidney or the less involved of the two kidneys. As to the making of repeated pyelograms of patients suffering with renal tuberculosis, it is our opinion that cystoscopic examination should be kept at an absolute minimum, as it is usually very painful to the patient and may produce actual harm. Dr. Braasch and I recently reviewed the last 100 consecutive cases of renal tuberculosis in which operation was performed at the Mayo Clinic (Emmett, J. L., and Braasch, W. F.: Has Excretory Urography Replaced Pyelography in the Diagnosis of Renal Tuberculosis? *J. Urol.* 40:15-23 [July] 1938). We found that the trend in diagnosis was definitely away from retrograde pyelograms. Most diagnoses were made on the basis of an excretory urogram and examination of the ureteral specimen of urine from the good kidney. In an effort to avoid unnecessary cystoscopic examinations, a group of urologists is beginning to advocate diagnosis by excretory urograms alone in most cases of renal tuberculosis. Whether late postoperative results by this method of diagnosis will justify its continuance time alone will tell.

THE CERVIX UTERI IN OBSTETRICS  
AND GYNECOLOGY

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Recognition of the intimate relationship of obstetrics and gynecology has come a long way since male midwives were first admitted to the birth rooms and since Marion Sims laid the foundations for modern gynecology.

In the truly great teaching centers and in most important hospitals it has long since been recognized that obstetrics and gynecology are twin specialties and should be taught together and so far as possible practiced together. It is true that most obstetric patients are and should continue to be cared for by men in general practice. The general practitioner who does obstetric work should be gynecologically trained and able to evaluate the gynecologic problems of his patients.

The interlocking pathology and principles of treatment of the cervix uteri demonstrate this unity well. The cervix is not merely an appendage protruding into the vagina. It is a distinct structural and functional entity. Its disorders may be related to its role in obstetrics or gynecology or both. This concept is vital to intelligent treatment.

The cervix is the conic or cylindric termination of the uterus, usually 3 cm. long. Of this two thirds protrudes into the vagina, the portio vaginalis, and one third is the so-called supravaginal portion.

The anatomic landmarks between the cervix and the corpus uteri are the reflection of the vesico-uterine peritoneum, the level at which the uterine arteries branch and the narrowing of the lumen of the organ at the anatomic internal os.

The isthmus uteri or pars intermedia, formerly a debatable subdivision, is now accepted and identifiable. It is essentially the supravaginal portion of the cervix. It extends downward for about 8 mm. from the level of the "anatomic internal os" to a point where the lining of the canal becomes abruptly cervical in character, the "histologic internal os."

The structure of the cervix, unlike that of the muscular corpus uteri, contains little muscle but much connective and elastic tissue. It is comparatively firm and unyielding. The superior end, the isthmus, is more muscular like the corpus but somewhat softer. This gives it the effect of a double hinge, which permits of ready backward and forward displacement of the corpus in the pelvic cavity. Whoever practices obstetrics must be familiar with the remarkable softening of the zone between corpus and portio in early pregnancy, the "Hegar sign." Again in late pregnancy and labor there appears the striking phenomenon of formation of the "lower uterine segment," that thinned out zone between the contractile corpus and the dilating cervix. These alterations involve the same segment of the uterus, the isthmus uteri.

The cervical canal extends from the external os to the anatomic internal os, is narrowest at these two points, averaging 4 mm. in diameter, and is slightly spindle shaped, averaging 7 mm. transversely at its widest point. In the formation of the cervix the ante-

rior and posterior walls are the stoutest. This becomes striking on examination of the postpartum cervix, and after involution the canal is found to be much wider as a result of the yielding and overstretching of the lateral walls. Histologically the lining membrane of the cervix is characterized by the presence of mucus-secreting glands which point downward and toward the canal and by the absence of cilia. The mucosa of the isthmus resembles that of the corpus. It can be distinguished by the direction of the glands. Those of the corpus point downward and toward the cavity and those of the isthmus upward and away from the canal.

The most striking histologic fact in connection with the cervix deals with the changes at the external os. The forward and backward interplay between the cuboidal cervical mucosa and the squamous epithelium covering the portio, with the external os as the prize, begins in fetal life. At the seventh month the canal of the cervix is lined by squamous epithelium. At birth the endocervix has pushed back the squamous epithelium beyond the external os and onto the portio in approximately 30 per cent of female infants, the so-called congenital pseudo-erosion. Within the first year of life in most of these infants the squamous epithelium acquires the mastery and the external os becomes the dividing line. Again at puberty a secondary physiologic pseudo-erosion may occur, which likewise tends to recede. This struggle continues throughout life.

In adolescence and maturity the epithelium covering the portio is subjected to the hypersecretions of the cervix which accompany certain constitutional diseases and to the irritation of cervical discharges due to inflammation. In either case the squamous epithelium is macerated, and the red mucus-secreting endocervix advances to erosion, which may be small and superficial or huge, furrowed and even papillary. Lastly, the cervix which has been traumatized in labor heals with gaping, gradual eversion, ectropion and erosion.

Postmenopausal atrophy of the corpus and cervix uteri is effected by two distinct influences. Atrophy of the corpus and its endometrium results from disappearance of the ovarian stimulus. Diminished circulation produces gradual atrophy of the cervix but to a much smaller degree than the shrinkage of the corpus. The endocervix retains its mature form and function (vaginal lubrication), since the cervix is not under the direct influence of the ovarian stimulus.

Fertilization, pregnancy and labor proceed normally only when all the organs involved are normal in structure and function. For fertilization the cervix should point posteriorly at right angles to the vaginal axis. It should not descend to the level of the ischial spines. The portio vaginalis should be covered right up to the external os by the smooth squamous vaginal epithelium. The external os should be sufficiently patulous, the mucous secretion from the endocervical glands should be distinctly alkaline and the canal itself should be slightly spindle shaped, terminating 3 cm. above the external os at the narrow internal os. At the time of orgasm this structure dips into the pool of semen deposited in the posterior vaginal fornix, and its alkaline mucosa forms a pathway of escape for the spermatozoa from the deadly acid secretion of the vagina.

With the foregoing in mind, it is easy to understand that retroflexion, retroversion and prolapse may render fertilization difficult or impossible. This type of infer-

tility may be overcome by the intelligent selection and competent execution of a corrective operation. The conduct of the ensuing labor should be so contrived as to preserve the operative results previously achieved.

The persistence of congenital pseudo-erosion or the development of pseudo-erosion after puberty, the erosion produced by inflammatory destruction of the epithelium covering the portio and its replacement by the endocervical epithelium, cervical laceration in labor with resultant eversion and erosion formation, all act as more or less insurmountable barriers to fertilization.

Endocervicitis not infrequently converts the normal alkalinity to an acid cervical secretion repellant to the spermatozoa. An endocervicitis may be the starting point of a puerperal infection with its chain of sequelae.

Inflammatory erosions with or without endocervicitis are often associated with urinary disturbances and with low backache. Appropriate treatment of the cervical lesion often results in complete relief of such symptoms.

Stricture of the cervical canal at any level may be congenital but is usually acquired. When inflammatory, it is usually below or above the spindle-shaped dilated zone, single or multiple, or it may affect the external os, "conglutinatio orificii cervicis externi."

Strictures may result from the trauma of curettage or following abortion, and application of radium may produce them. For demonstration of strictures of the cervical canal on specimens the frontal section is better than the sagittal section, as this lays the canal open in its widest diameter.

Each of these manifold lesions presents a separate gynecologic problem which may be solved in various ways. If the point requires further emphasis, this interlocking of obstetric and gynecologic problems justifies the bald assertion that no one can be a competent obstetrician without adequate training in gynecology and its converse.

Symptomless retroflexion and retroversion require no treatment. To facilitate pregnancy, however, if the malposition of the uterus is not maintained by adhesions a properly fitted pessary, removed and replaced monthly, may be a definite aid toward pregnancy.

The adherent corpus uteri can sometimes be dislodged and erected under anesthesia. When this fails, surgical correction is indicated. Formerly the Gilliam suspension operation or one of its modifications was the method of choice. It is still reliable when properly executed. Two points are especially important in this procedure. The short arm of the double loop of round ligament should not be more than 3 cm. long, so that the fundus uteri will sit snugly against the abdominal wall, and the point of implantation of the ligaments into the abdominal wall should be 4 cm. above the symphysis. If the attachment is placed much lower and pregnancy occurs, the uterus sometimes fails to expand evenly in the vertical axis and either an abortion follows or the pregnancy develops entirely at the expense of the posterior wall of the uterus.

It may be entirely adequate in selected instances to rely on shortening of the uterosacral ligaments, radical advancement of the bladder and other methods of shortening the round ligaments.

Surgical cure of prolapse of the uterus with preservation of fertility continues to tax the ingenuity of operators. Correct treatment of the cervix is vital to success. If an unduly elongated portion of the cervix

is preserved, the operation for prolapse is usually doomed to failure. If the cervix is amputated too close to the internal os, subsequent pregnancy usually ends in abortion or immature labor.

The parametrial fixation operation<sup>1</sup> has assumed first place in popularity. The important steps are denudation of an area of the anterior vaginal wall proportional to the size of the existing cystocele, if any; dislodgment of the bladder; amputation of enough of the cervix to reduce the overall length of the uterus to 8 cm., of which from 2 to 3 cm. should be cervix; parametrial fixation anterior to the cervix, and reconstruction of pubovesicocervical fascia. The perineal body, if relaxed by previous delivery, must likewise be thoroughly reconstructed. Another procedure which can be carried out vaginally is the Halban-Porges operation.<sup>2</sup> Here again the cervix must be reduced to proper length and the anterior peritoneal reflection opened after the usual vaginal dissection and upward displacement of the bladder. The anterior flap of the peritoneal reflection which overlies the back wall of the bladder is now pulled into the vagina until it no longer advances. The fundus uteri is then sutured transversely against this anterior part of the peritoneum as close to the parieto-vesical angle as possible. The peritoneal opening is then closed, a strong reconstruction of the anterior vaginal wall is accomplished and the perineal body is reconstructed.

Formerly the treatment of ectropion and erosion consisted in repeated application of various chemicals aimed at the destruction of the misplaced cuboidal epithelium. It should be noted that in all instances of erosion islands of squamous epithelium remain in the zone of the lesion and aid in the rapid epithelization of the portio when the overlying encroaching tissue is destroyed.

The modern method of treatment for ectropion and erosion is complete destruction by the electrocautery, first carried out by Hunner<sup>3</sup> in 1906. Originally it was thought that radial destruction with preservation of the intervening epithelium was necessary. Long experience has demonstrated that complete destruction, until a black eschar is achieved, is entirely safe. This can be carried out as a single office procedure and requires no anesthesia, local or general. Similarly, endocervicitis can be cured or so completely subdued with the platinum loop electrocautery or the Cherry electrode or by electrocoagulation as to permit the return of normal secretory activity.

In fifteen years of office cauterization with the nasal tip cautery I have observed only two instances of late hemorrhage, both controlled by recauterizing, and only one instance of stricture.

Strictures resulting from any of the causes previously given must be treated by vigorous dilation, the best type of instrument being the graduated metal Hegar dilators.

When pregnancy has been established, the cervix becomes increasingly important. It is the living barricade and barrier. It locks the developing fetus and its protective fluid chamber within the corpus cavity. It absorbs the shock of impact which may accompany coitus. It accumulates the mucus which is no longer carried out with the menstrual flow and so provides an effective plug against bacterial invasion of the corpus cavity. If now the cervix is too short, whether congenitally or because of operative or traumatic destruc-

1. Frank, R. T.: *Am. J. Obst. & Gynec.* **29**: 240 (Feb.) 1935.  
2. Mestitz, Walter: *Surg., Gynec. & Obst.* **54**: 663 (April) 1932.  
3. Hunner, G. L.: *Treatment of Leukorrhea with Actual Cautery*, *J. A. M. A.* **46**: 191 (Jan. 20) 1906.

tion, or if previous trauma in labor has left it gaping widely, it is easy to understand how abortion may ensue.

Chronic infection of the cervix in the presence of pregnancy has heretofore received little attention. The fear of producing abortion has kept physicians from attempting any direct attack on the lesion. Yet Miller and his associates<sup>4</sup> reported in 1930 the treatment of erosion and endocervicitis in 2,000 cases by electrocauterization of the cervix and the canal. Their series was limited to patients up to the twenty-eighth week. The procedure always caused contractions at the time, but there was only one abortion which they felt was due to the cauterization. They reported no obstetric abnormality traceable to the cauterization, a marked decrease in puerperal morbidity, no sepsis and no recurrence of the erosion after delivery. Absence of any recurrence of erosion in 2,000 deliveries is difficult to understand. Aside from this question, however, the preservation of pregnancy and the removal by cautery of a direct source of uterine infection may prove to be a tremendous step in the reduction of maternal morbidity.

Passmore<sup>5</sup> confirmed these results in 1932. He found only sixty patients among 600 who required cauterization, twenty-four with severe and thirty-six with minor lesions.

Effacement of the cervix, that is, the shortening of the long axis and its eventual merging into the lower uterine segment, may begin weeks before the onset of labor. Dilatation of the external os usually follows the dilatation of the cervical canal. The external os may persist as a pinhole-sized os (conglutination) after the cervix is completely effaced and the lower uterine segment is well thinned out. This condition may simulate complete dilatation on rectal examination and may result in application of the forceps to the head, the blades being forced through the uterine cap with inevitable severe injury.

When the cervix has been lacerated in previous labor the external os is no longer a dimple or slit but is a widely gaping orifice bordered by more or less hypertrophied everted anterior and posterior lips, with scar tissue in the lateral angles. This type of multiparous cervix is responsible for precipitate labor, for extensive additional cervical lacerations if the patient is permitted to bear down before dilatation is complete and for incarceration of the edematous anterior lip between the head and the symphysis, which, unless released by upward dislodgment, may prevent delivery and result in necrosis or avulsion of the incarcerated cervix. In this connection it is interesting to note that there are seventeen recorded instances of spontaneous annular amputation of the cervix in labor.

The issue of rectal versus vaginal examination in the conduct of labor should not exist. A single vaginal examination properly carried out either in the home or at the hospital is no menace to the safety of the mother and is the only way in which the physician of average experience can orient himself as to all the accessible factors involved in the delivery. Subsequently the rectal approach will tell the story of the disappearing cervix and confirm the level of the head. Further vaginal examinations may be done only for special indications.

Inspection of the cervix immediately after delivery reveals a massive organ hanging loosely in the upper

part of the vagina. The anterior and posterior segments are heavy, while the lateral zones are markedly thinned out. Lacerations when present are usually in the thin lateral walls of the cervix. The distance from the external os to the top of the vagina at this time is approximately 10 cm. A tear of 2 cm. in the lateral zone will, when involution is completed, be nothing more than a physiologic nick at the external os. Moreover, attempted suture of these thin edges is usually only a gesture. The patient in whom labor has progressed spontaneously and normally to complete effacement and dilatation, with subsequent advance of the head to the pelvic floor, rarely sustains a major injury of the cervix. Major injuries should be repaired promptly.

Danforth<sup>6</sup> reported the results of immediate inspection of 904 cervixes after delivery, excluding instances of bag induction, manual dilation and cesarean section. He found laceration in 102, sixty-nine primiparas and thirty-three multiparas. In fifty-eight the tear was less than 2 cm. and not sutured. In forty-four the tear was more than 2 cm. and in thirteen of these ranged from 3 to 5 cm. In these forty-four the tear was repaired, an incidence of only 4.5 per cent. This conforms to my own observation and practice. The inspection of the cervix as a routine after delivery is therefore superfluous in most instances and increases the risk of morbidity.

When injury is suspected because of operative procedures and inspection reveals a laceration exceeding 2 cm., repair should be carried out with loosely tied interrupted catgut sutures, the first being placed above the angle of the tear. For cervical bleeding one or more sutures may need to be tied more tightly. Repair of old cervical injuries at the time of subsequent delivery is not advisable. The risk of creating atri of infection is greater than the alleged advantage of sparing the patient a subsequent hospitalization.

Massive edema of the postpartum cervix has been reported many times. It must be differentiated from prolapse and inversion of the uterus. With bed rest and nonintervention the edema disappears in from ten days to three months.

Operative correction of cervical pathologic conditions varies with the lesion and the desired objective. Certain underlying principles may be enunciated. Simple birth injuries which are symptomless and are not accompanied by inflammatory changes require no treatment. If the patient is to retain her childbearing capacity, birth injuries requiring attention must be repaired in such manner as to avoid undue foreshortening of the cervix. If this is not an objective, other types of repair are available in which preservation of the proper length of the cervix and endocervix is no longer necessary. If the lesion is essentially the result of inflammatory changes with the development of multiple cysts and florid erosions, the cautery is adequate. It has completely displaced the Schroeder operation in my practice. For deep laceration with heavy scar formation, excision and approximation are indicated. If there is gross involvement of the endocervix as well as multiple cyst formation on the portio, the Sturmdorf operation—cone-shaped excision with utilization of the portio as a new lining for the canal—is excellent. For simple hypertrophy and elongation, low or high amputation is

4. Miller, H. A.; Martinez, D. B., and Hodgdon, M. E.: *Pennsylvania M. J.* 34: 708 (July) 1931.

5. Passmore, B. H.: *Texas State J. Med.* 27: 716 (Feb.) 1932.

6. Danforth, W. C.: *Am. J. Obst. & Gynec.* 15: 505 (April) 1928.



selected in accordance with the patient's wishes concerning pregnancy.

Each of these operative procedures is of the nature of a plastic surgical measure and calls for a nice sense of proportion and fit to accomplish a satisfactory end result. Still the selection of the appropriate operation is more important than extreme dexterity in its execution. The sound judgment of the trained "gynecician" is worth more to the patient than a cosmetic stub of cervix which will no longer protect pregnancy.

In the actual technic several points are important. Interrupted sutures are preferable to continuous or lock stitch sutures. They should be placed approximately 1 cm. apart and should be tied for apposition only. The suture material should be well chromicized no. 2 catgut. Occasional late hemorrhage has influenced many operators to utilize silkworm gut for the deep sutures in this kind of work. Tested catgut serves equally well and obviates the necessity for subsequent removal.

Benign tumors of the cervix, though infrequent, are usually fibromyomas. The accepted treatment is enucleation. In this connection a word of caution is advisable. Many patients with this type of growth are anemic because of protracted menstrual bleeding, with resultant lowered resistance to infection. The cervix is richly supplied with lymphatic vessels which drain into the broad ligaments. Death from sepsis may follow simple enucleation of such a tumor of the cervix. The patient should be prepared by a preliminary blood transfusion, and the field of operation should receive the most scrupulous preoperative preparation.

Carcinoma of the cervix holds first rank among all the obstetric and gynecologic causes of death. Hinselmann's<sup>7</sup> colposcope was devised to reveal tiny lesions of the cervix which might be incipient carcinoma and promptly curable. Schiller's iodine test<sup>8</sup> was aimed at the same objective. Each of these devices, to be effective, must be used as a routine, with biopsy of any suspicious areas. When the microscopic picture is clear-cut the lesion is usually one which should have aroused suspicion without either one of these aids. Other specimens, studied because they do not take up iodine, may show what Schiller called the preinvasive stage of carcinoma. Unfortunately this classification is not generally accepted by pathologists. I have found the colposcope unnecessary and the iodine test inadequate.

For the cure of carcinoma of the cervix the old issue of surgical measures versus irradiation scarcely exists any longer. Treatment with radium or roentgen rays or both has almost completely displaced surgical methods in the hands of the most experienced specialists here and abroad. Choice of treatment based on types of cells—that is, whether they are radioresistant or radio-sensitive—has been found fallacious with both types so often that type is really no longer a criterion.

Clinically, if the lesion is truly incipient with no detectable involvement of the deeper part of the cervix or the parametrium, hysterectomy followed by irradiation may still be justifiable.

The menace of the cervical stump after subtotal hysterectomy has been a source of some concern and an argument in favor of routine total hysterectomy. The Mayos<sup>9</sup> have regarded it as a potential focus of infection resulting in keratitis, iritis and arthritis of the small joints. If this were so, although atrophy is the common fate of the stump, the source of infection could readily be eradicated by vigorous use of the cautery.

Masson<sup>10</sup> reported ninety-nine instances of carcinoma in twenty years at the Mayo Clinic and expressed advocacy of total hysterectomy as a routine. He reported a mortality of 1.2 per cent among 3,085 subtotal hysterectomies and of 1.8 per cent among 1,588 total hysterectomies. He stated that this increased mortality was negligible. Actually, however, it was a 50 per cent increase. It means that if all the subtotal operations had been total there would have been fifty-five deaths instead of thirty-seven. Polak culled only 256 cases from the world literature up to 1920, and it is to be doubted whether this extremely low incidence of carcinoma of the stump justifies the increased mortality almost certain to result from widespread indulgence in total hysterectomy as a routine.

It has been my aim throughout this brief analysis to convey the picture of a structure which, though a part of the uterus, is as distinct from it in function, pathology and treatment as the hypophysis is from the brain. The full significance of this picture is best understood when viewed through a binocular, one side labeled obstetrics and the other gynecology.

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#### ABSTRACT OF DISCUSSION

DR. EDWARD A. SCHUMANN, Philadelphia: I shall confine myself to one or two points of Dr. Baer's paper. The management of the old injured, infected and lacerated cervix has undergone a continuous change during the past thirty-five years. At the beginning of this period the methods for the relief of this lesion consisted in the deep, widespread Schroeder amputation or the entirely inadequate Emmett trachelorrhaphy, leaving a canal of presumably infected glandular tissues. These procedures were superseded by the Sturmdorf operation, and recently since the appearance of the electric conization knife I have found it adequate to abandon all operations for repair of the lacerated cervix and to depend for its relief on a wider or lesser excision of the tissue with the electric knife. The deal of nonsense which has been spoken and penned about the dangers of vaginal examination is most unfortunate and unbelievable. This whole matter has been so misunderstood, in my opinion, that Dr. Baer's statement that "a single vaginal examination, properly conducted, causes no harm and is no menace to the parturient woman" was delightful. His second statement was to the effect that routine observation of the cervix after delivery is not necessary. For ten years I have followed and observed every cervix of every parturient woman, and they presented every degree of laceration. Those presenting any degree at all were subjected to immediate repair. Gradually I found that but little good was done by this procedure, and while I did not find any increase in morbidity as a result of it, it has been almost entirely abandoned by clinicians unless some indication has rendered such observation important. With regard to the effect of chronic cervicitis and endocervicitis with leukorrhea on the production of puerperal morbidity, I am considerably interested. My associates and I are now conducting a series of observations on this matter in an attempt to prove our impression that puerperal morbidity is not enhanced thereby. Another point of Dr. Baer's that I wish to applaud is that the colposcope

7. Hinselmann, H.: *Zentralbl. f. Gynäk.* 51:901, 1927.

8. Schiller's iodine test: A. Clean cervix and inspect for (1) color of mucous membrane, (2) presence and sites of leukoplakia, (3) presence of erosions and (4) color of eroded areas. B. Bathe cervix for one minute in a solution made of 1 part tincture of iodine, 2 parts potassium iodide and 300 parts distilled water and inspect for (1) normal epithelium (is pink; turns mahogany brown), (2) normal erosion (is pink or red; remains pink or red), (3) carcinomatous epithelium (may be pink or white; turns pearly white) and (4) connective tissue (is pink; remains pink). C. A white patch is suspicious and must be examined histologically. It may be (1) carcinoma, (2) syphilis, (3) hyperkeratosis or (4) a scar.

9. Mayo, C. H., and Mayo, Charles, Jr.: *Ann. Surg.* 92:1215 (June) 1931.

10. Masson, J. C.: *Am. J. Obst. & Gynec.* 14:486 (Oct.) 1927.

is unnecessary and the Schiller test inadequate. I should like also to thank Dr. Baer for two statements he did not make. He did not call the cervix the "tonsil of the uterus" and he did not ascribe to this purely connective tissue substance with its thin layer of mucosa all the ills to which the possessor of a cervix is susceptible.

DR. GEORGE W. KOSMAK, New York: Dr. Baer called attention to the importance of the cervix in pregnancy. Although, as he states, it is a part of the uterus, there is a distinct difference in its physiology and pathology. I feel that in many cases insufficient attention is given to this structure when malignancy has been excluded. Chronic inflammations of the cervix, however, give rise to a multitude of symptoms the etiology of which may not be recognized as residing in this organ but which frequently call for radical rather than palliative measures, such as local applications and linear cauterization. I believe the latter has been much abused and that it is applicable only for superficial lesions, such as the so-called erosions of the vaginal portion. Deep seated infections of the canal are not satisfactorily eliminated, and if deeper cauterization is required the resultant scar formation is undesirable. The removal of a conical mass of cervical tissue with the electrocautery, as developed by Hyams and others, is satisfactory but requires special aptitude and skill. I have had excellent results from the Sturmdorf procedure, and subsequent pregnancy is rarely interfered with. The behavior of the diseased cervix in pregnancy may be given further consideration. The polypoid erosions may undergo development in early pregnancy and the resultant bleeding, especially after coitus, leads to the diagnosis of an impending or inevitable abortion, with later resort to curettage. In every case of bleeding during this period, visual inspection of the cervix is demanded and the bleeding can frequently be checked with the platinum loop brought only to a dull red heat. A white heated point usually increases the bleeding. The treatment can be repeated at intervals of from seven to ten days, supplemented with appropriate suppositories, tampons and douches. I have never seen abortions follow this procedure. Bleeding from the cervix in the later months of pregnancy may simulate placenta praevia: again visual inspection is demanded but local treatment is less satisfactory. Naturally, placenta praevia must be definitely excluded, which is not always possible, particularly in the marginal or lateral types, as a cervix previously diseased is apt to undergo much earlier softening. Dr. Baer questions the advisability of immediate repair in the milder degrees of lacerations and with this I would agree, as there is more danger of local infection and possible interference with lochial drainage. Therefore the apparent depth of a tear is of less importance as a deciding factor for repair than hemorrhage.

DR. GOODRICH C. SCHAUFFLER, Portland, Ore.: I thank Dr. Baer for his scholarly and sound presentation. Ten years ago Albert Mathieu and I made a survey of everything in the literature in relation to the caustic and cautery treatment of the endocervix. We found that there occurred an interesting cycle. In 1840 interest in the use of caustics and the cautery on the endocervix began to rise; from that time on there were increasing case reports in the literature, coming to a peak in about forty years (1880). A subsequent peak was reached several years later by the incidence of stasis, cervical occlusion and difficult labor following these treatments. These were simply as reported in the literature and may not represent the true condition; but in view of the modern tendency to radical, so-called office procedures on the endocervix—conization, cauterization, deep really surgical procedures—I call attention to this historical cycle for what it is worth. I was interested in Dr. Baer's presentation of the mode of growth of the epithelium, the cuboidal epithelium, growing down from the uterus and invading the portio vaginalis. A slide from the genitalia of a stillborn fetus shows the vagina and the endocervix with the usual roles of "harbors of infection" definitely reversed. There is a smooth endocervix with practically no cervical glands. The stratified epithelium is still high in the cervix and the vagina itself is rugose, cryptiform and poorly drained. I call attention to this in relation to the infectivity of the immature cervix, which I believe is practically noninfectible from the point of view of the glandular structure involved.

## TREATMENT OF PREERUPTIVE MEASLES WITH CONVA- LESCENT SERUM

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It has been established that measles convalescent serum will prevent or modify measles in children intimately exposed to it if a sufficient amount of this serum is given intramuscularly by the fifth day after exposure. Sometimes this is effective up to the eighth day after exposure. The efficiency of the prophylaxis has been confirmed by observations in large series of cases all over the world.<sup>1</sup>

Sporadic attempts also have been made to mitigate measles even after it has reached the active stage by administering convalescent serum before, during and after the appearance of the eruption. Most investigators<sup>1</sup> have stated that these attempts were unsuccessful.

It also has been reported by many authors<sup>2</sup> working on experimental virus disease that once a pathogenic virus has invaded the body cells it is impossible for a therapeutic serum to cause any beneficial effect. The etiologic agent of measles in the light of many studies is probably a virus.

In spite of the discouraging reports of these therapeutic efforts and of the skepticism shown that any serum will mitigate a virus disease once it has reached the active stage, we felt that another, more systematic, therapeutic attempt to give convalescent measles serum in the preeruptive stage would be justified. If effective, such therapy might lower the mortality of measles, occurring in the weak, debilitated infant or child or in persons who have just recovered from an infectious disease or those suffering from an acute or chronic disease.

### MATERIAL AND PROCEDURE

In the spring seasons of 1937 and 1938, children admitted to the Willard Parker Hospital in the preeruptive stage of measles were given varying amounts of convalescent serum. Children who were admitted for some other illness and in whom measles developed while they were in the ward were similarly treated. At the time of injection, definite Koplik spots were present in all patients and none of the children had previously received any measles convalescent serum. In all, twenty-four children were so treated. The serum was administered intravenously. In six of these children, at the time of the intravenous injection, additional serum was given intramuscularly. Fourteen of these children were 3 years of age or under.

Nine other children were given an intravenous injection of an equal volume of normal adult serum during the preeruptive stage.

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The authors had the cooperation of Dr. William Thalheimer, director of the Manhattan Convalescent Serum Laboratory.

From the Willard Parker Hospital for Contagious Diseases, the Department of Hospitals and the Manhattan Convalescent Serum Laboratory.

1. Thomson, David, and Thomson, Robert: The Role of the Streptococci in Measles, *Ann. Pickett-Thomson Research Lab.* 7: 193 (July) 1931 (comprehensive bibliography).

2. Rivers, T. M.: Recent Advances in the Study of Viruses and Viral Diseases, *J. A. M. A.* 107: 296 (July 18) 1936.

Four other children were given concentrated normal serum<sup>3</sup> intravenously, also during the preeruptive stage. The convalescent serum used by us was processed according to the regulations of the U. S. Public Health Service. The serum obtained from thirty individual bleedings was pooled, so that the age of the serum averaged not more than sixty days after the onset of the measles in the donors.

Normal adult serum was prepared in exactly the same way, the source, however, being healthy normal adults none of whom had recently been ill. Most of these adults had had measles during childhood.

The concentrated serum used was prepared according to the method described by Thalhimer.<sup>3</sup> It was concentrated to one third of its original volume. It was prepared separately for the four different blood types.

RESULTS

Modified measles has a much milder course than the usual measles. The patient is not very ill; the fever is at a lower level and its duration is short. The catarrhal stage is less severe. The eruption is modified

Summary of Results Obtained with the Use of Measles Convalescent Serum

Number of Patients	Amounts in Cc. (at Least)		Clinical Course		
	Intra-venously	Intra-muscularly*	Modifi-cation	Questionable Modifi-cation	Failure
12	50	..	10	..	2
4	40	..	3	..	1
1	40	15	1	..	..
1	40	10	1	..	..
2	30	..	..	1	1
2	30	20	2	..	..
1	25	..	1	..	..
1	20	20	..	..	1

\* Intramuscular injection was given at the time of the intravenous injection.

in that the maculopapular lesions are discrete, scattered and confined mostly to the face. The cough is not as severe and is of short duration. The posteruptive illness is of short duration, and complications are unusual. Recognition of the modification of the clinical

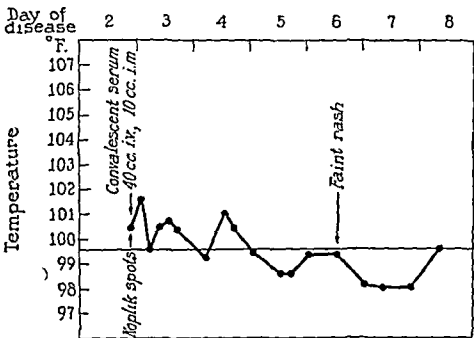


Chart 1.—The temperature curve in case 17. Measles serum was given intravenously and intramuscularly during the preeruptive stage. A faint rash was noted four days after injection. The temperature was never over 102 F.

course of measles can be made with a fair degree of accuracy.

Measles can be modified in young children if about 5 cc. of convalescent serum is injected intramuscularly from five to eight days after exposure. Once active clinical symptoms are present, larger doses of the serum

would be necessary to modify the disease. We decided to administer the serum intravenously in order to obtain immediate widespread distribution and in the hope that the serum would act more efficiently.

Intravenous injection of pooled human serum, particularly in scarlet fever, sepsis and hypoproteinemia, is a standardized procedure. This extensive experience

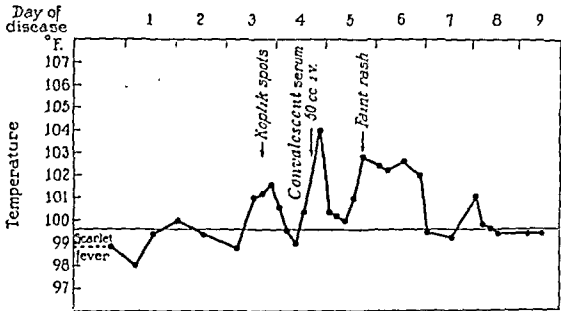


Chart 2.—The temperature curve in case 19. Fifty cc. of measles convalescent serum was given intravenously during the preeruptive stage. A faint rash appeared the next day. There was a definite modification of the measles, and the fever continued for two days after the appearance of the rash.

has proved that only rarely does any untoward reaction occur. We felt sure, therefore, that no risk was being taken in the intravenous administration of large quantities of pooled human serum. Empirically we decided to give 50 cc. to the first few patients admitted. From the data thus obtained we could estimate dosage on subsequent patients.

As noted, twenty-four children were injected with measles convalescent serum. Of these, ten patients received the serum two or more days before the appearance of any rash, and the remaining fourteen one day before.

The course of the measles was definitely modified in ten of the twelve children who received 50 cc. or more intravenously. It was definitely modified in five of the six children who were given from 40 to 45 cc. intravenously. Four children received 30 cc. intravenously. There was modification in only the two of the four who were given an additional 20 cc. intramuscularly. There was modification in one child who received 25 cc. intravenously but none in the child who received 20 cc. intravenously and an additional 20 cc. intramuscularly. The intramuscular injections were given at the time of the intravenous injections. The results are given in the accompanying table.

There was a total of five failures and one questionable modification in the twenty-four children treated. From the data obtained it would appear that in order to obtain modification about 40 or 50 cc. of the measles convalescent serum should be injected intravenously at least one day before the appearance of the eruption (charts 1 and 2).

The course of the measles was modified, in that these children were not very ill. The rash was not profuse and was confined largely to the face and upper part of the chest. On the face the rash was morbilliform and was discrete elsewhere. The cough was not distressing and ceased in a few days. In most of the cases fever persisted for about two days after injection (as compared with an expected duration of three or four days). The maximum height of the temperature was perhaps a little less than is to be expected in unmodified measles. If pneumonia was not already present on admission, none of the patients receiving

3. Thalhimer, William: A Simple Inexpensive Method for Concentrating Serum Under Sterile Conditions, Proc. Soc. Exper. Biol. & Med. 37: 258 (Jan.) 1938.

measles convalescent serum gave subsequent evidence of pulmonary involvement.

As mentioned, twelve children received intravenous injections of 50 cc. or more of convalescent serum. In order to ascertain whether the course of the disease could be further influenced, four of these patients were given a second injection a day after the first and one patient was given two additional injections on successive days. This treatment seemed to have some additional effect. The rash did not appear until the injection of the serum was stopped, and it was sparse and modified. We had the impression that the appearance of the rash was being retarded by these successive injections (chart 3).

Four of the twenty-four children receiving convalescent measles serum were severely ill at the time of the discovery of measles. One had peritonitis, the second widespread pneumonia, the third severe rheumatic fever and the fourth severe croup. We feel that their recovery was favorably influenced by modification of the measles.

#### REPORT OF CASES

CASE 6.—V. D., a boy aged 5 years, was admitted April 11, 1937, with a severe nondiphtheritic croup; Koplik spots were noted. He was examined with a laryngoscope; no membrane was present but intubation was necessary. The day after admission 50 cc. of measles convalescent serum was given intravenously. The next day he was much improved and a faint measles rash appeared on the face and the chest. On the same day the tube was removed. A pneumonic infiltration was now present in the right lower lobe. His condition was satisfactory for four days, when the croup returned and intubation was again done. The tube was removed the next day; he improved within a few days and recovered rapidly.

CASE 22.—E. F., a girl aged 13 months, admitted April 28, 1938, had been discharged from Willard Parker Hospital six weeks before. She had been ill with whooping cough and pneumonia. She continued to cough at home. Eight days before the present admission, the child was ill with varicella. Six days later she became very ill, with a severe paroxysmal cough and extreme difficulty in breathing. On admission the child was severely ill; she was cyanotic and the respirations were shallow and rapid. Koplik spots were present. She was put in an oxygen tent. Physical examination and roentgenograms of the chest showed a diffuse pneumonic infiltration. Soon after admission 50 cc. of measles convalescent serum was

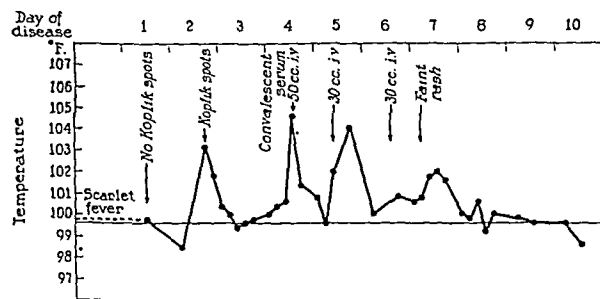


Chart 3.—The temperature curve in case 2. Measles convalescent serum was injected intravenously on three successive days during the preeruptive stage. No rash appeared until twenty-four hours after the last injection. The measles was definitely modified.

given intravenously. Another 50 cc. was given the next day. The child's condition improved, and two days after admission a faint rash appeared. The temperature dropped to a normal level. It was found necessary, however, to keep the child in an oxygen tent for a full week. Fine rales heard at the bases of both lower lobes persisted for an additional ten days after removal from the tent (chart 4).

CASE 23.—T. R., a boy aged 4½ years, was admitted May 2, 1938. Four days before admission he had been admitted to

another hospital for an acute attack of appendicitis. At operation a gangrenous appendix with diffuse peritonitis was found. Koplik spots were seen on the third postoperative day and the child was transferred. On admission he was very ill and was given 50 cc. of measles convalescent serum intravenously. The measles was definitely modified, and his temperature returned to normal within three days.

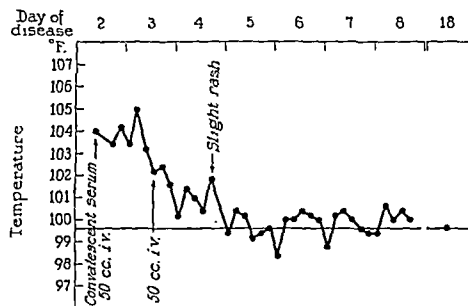


Chart 4.—The temperature curve in case 22. The child was admitted with a severe, widespread pneumonia. Convalescent serum was injected intravenously on two successive days. The measles was definitely modified, the temperature dropped to a lower level and the child improved clinically.

CASE 14.—L. H., a boy aged 9 years, had rheumatic fever with a severe cardiac insufficiency and was admitted to Willard Parker Hospital April 23, 1937, because Koplik spots were found. On admission the boy was very dyspneic, and coarse rales were heard throughout both lungs. He was given 60 cc. of measles convalescent serum intravenously and two days later a faint rash appeared with definite modification of the measles. The child improved and he was returned to the hospital of original admission.

It was important to ascertain whether the injection of an equal volume of normal adult serum would have the same effect on preeruptive measles as the injection of measles convalescent serum. Since nearly all of the donors of normal serum had had measles during childhood, the normal serum contained a small amount of measles protective substance. Nine children were given 50 cc. of normal adult serum intravenously. In seven of the patients the measles was not modified and in two there was perhaps slight modification. In fact, in two of the children clinical and roentgen evidence of pneumonic infiltration subsequently developed. It is obvious therefore that, once symptoms of measles have appeared, the intravenous administration of 50 cc. of normal serum does not modify the disease.

It is necessary to use about four times as much normal pooled serum to cause the same prophylactic effect as is secured by measles convalescent serum. We wondered whether normal serum given in the same ratio during the preeruptive stage would be effective also in the modification of the measles. Assuming this ratio, it would be necessary to inject from 160 to 200 cc. of normal serum in order to obtain modification. This obviously is a large quantity.

We had available some normal serum concentrated to one third of its original volume by the method described.<sup>3</sup> From 50 to 70 cc. (equivalent to from 150 to 210 cc. of unconcentrated normal serum) was given intravenously during the preeruptive stage. Four children were treated with this concentrated normal serum. In three of these children the serum was injected the day before the appearance of any rash. There was some modification of the disease in only one of these three children. On the other child the rash did not appear until four days after the injection and was scarcely visible.

It is our impression that, once measles has developed, concentrated normal serum is not as efficient as measles convalescent serum, even if given in the ratio discussed. We realize that it is hardly fair to draw conclusions from experience with only four patients.

We hope some time in the future to report on the treatment of severe pneumonia occurring mainly in the late eruptive and posteruptive stage of measles. Ten children with pneumonia and measles were injected intravenously with from one to three large doses of measles convalescent serum or scarlet fever convalescent serum. Thus far the results have been of questionable value.

#### COMMENT

Since in virus diseases specific therapy is of little avail once active infection is present, it seemed surprising to us that this dictum does not apply to measles. The etiologic agent of measles is probably a virus. It was of further interest to note that by giving convalescent serum on successive days we thought it could further influence the clinical progress of the disease. The eruptions did not appear until the serum was stopped.

Zinsser<sup>4</sup> states that the immunologic difference between virus infection and bacterial invasion may be eventually explained by the intracellular position of the former. It would appear that virus multiplication requires the cooperation of the body cell (intracellular) metabolism. The cause of injury in virus diseases appears to depend on the metabolism of the invaded cells. Bacteria, in contrast, can multiply and thrive in the body cells, in intercellular fluids and on artificial mediums. Bacteria are more strictly parasites. This difference between viruses and bacteria may be the reason why immune serum can act more efficiently on bacteria. Filtrable viruses apparently are protected by the invaded cell, making it more difficult for the injected serum to act.

In our experience thus far the indications for this therapy apply to the following groups: weak, debilitated and malnourished infants or children; those who have just recovered from one or more of the infectious diseases of childhood, particularly whooping cough, and children who at the time of the development of measles were suffering from a severe, acute or chronic disease, such as pneumonia, rheumatic fever or peritonitis.

Should measles convalescent serum not be available, a transfusion of 125 cc. of whole blood from a donor recently recovered from measles could be used. It should be simple in any community to secure a donor of this kind.

We have not given measles convalescent serum at the height of the eruption. However, we have received from many physicians reports of good results when such serum was given to very sick persons at the height of the eruption. Guibert and Lapeyre<sup>5</sup> and Armstrong<sup>6</sup> also report excellent results when the serum was given at the height of the eruption. We cannot yet evaluate the efficiency of this procedure since clinically it is known that very sick patients improve rapidly when once the rash has reached its maximum.

#### SUMMARY AND CONCLUSIONS

1. The intravenous injection of adequate amounts of convalescent measles serum, if given in the preeruptive stage of measles, modifies the course of the measles in most cases. Twenty-four children were so injected. In nineteen of these children definite modification was obtained.
2. The effective dose is from 40 to 50 cc. given at least one day before the appearance of the eruption.
3. The injection of convalescent serum on successive days seemed to have an additional effect.
4. Normal adult serum given in equal volumes to that of measles convalescent serum caused no modification.
5. The administration of from 150 to 210 cc. of normal serum concentrated to one-third its volume was effective in only one or possibly two of four patients.
6. There is no risk in the intravenous injection of large quantities of properly prepared pooled human serum.
7. This therapy is indicated especially under the following conditions: in weak and debilitated children, in those just recovered from whooping cough and other infectious diseases of childhood, and in those in whom measles developed during the course of another acute or chronic disease. Such children may thus be spared a severe attack of measles and perhaps avoid a fatal or a prolonged illness.

#### PLASTIC SURGERY IN CHILDREN

##### THE MEDICAL AND PSYCHOLOGIC ASPECTS OF DEFORMITY

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AND

E. HOYT DE KLEINE, M.D.

DETROIT

The past two decades have brought forth intensive campaigns in behalf of crippled and otherwise physically handicapped children of this country. Equally serious, but less widely publicized, are the childhood handicaps that are the results of deformity. By "deformity" we refer to those visible abnormalities which handicap their victims because of a peculiar appearance.

As examples of this group, we might cite harelip and cleft palate, facial birthmarks, saddle nose, hunchback, webbed fingers, crossed eyes, ptosis of the eyelid, disfiguring scars, lop ears, crooked teeth and contractures resulting from burns. Many of these are congenital deformities and others are acquired during childhood. Of the acquired group, many might have been prevented or minimized at their onset. In addition to efforts at prevention, the greatest service to such children is the work being done in the correction of such defects by plastic surgery. Plastic surgeons must, of course, give due credit to the achievements of orthopedists, dentists, ophthalmologists and dermatologists, whose efforts have made many other deformities amenable to treatment.

Although the effects of deformity are largely psychologic, the ultimate responsibility for their management generally falls on the shoulders of some physician. It is for these physicians that we present this summary of the pertinent facts relating to childhood deformities. Let it be said at the outset that we are not professional psychologists. We are primarily surgeons interested in

4. Zinsser, Hans: On the Nature of Virus Agents, *Am. J. Pub. Health* 27:1160 (Nov.) 1937.

5. Guibert, L. E. M., and Lapeyre, A.: Essai de traitement des formes graves de la rougeole par le sérum de convalescents, *Rev. serv. de san. mil.* 106:823 (June) 1937.

6. Armstrong, J. W.: Personal communication to the author.

the correction of these deformities and our discussion on psychology is derived from personal experience in the management of such cases.

#### PSYCHOLOGIC EFFECTS OF DEFORMITY

1. *Inferiority and Shame.*—The first and foremost mental effect of deformity seems to be that of inferiority and shame. Children are notoriously observant of the unusual. A great deal of undue attention is invariably directed at any cosmetic abnormality possessed by a

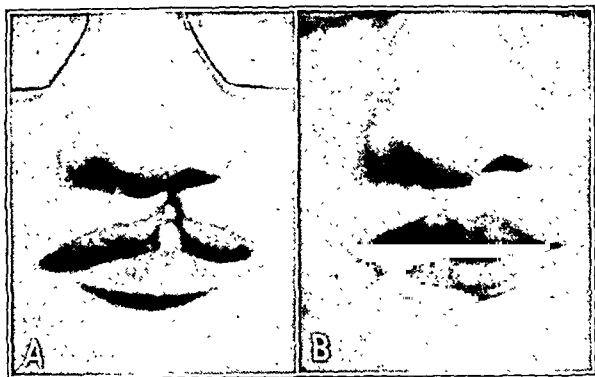


Fig. 1.—A, unrepai red single harelip in a girl in her teens. She became excessively self conscious of her deformity at about 10 years of age and quit high school during her freshman year, owing to embarrassment. Subsequently she stayed at home most of the time. B, same patient after repair of the lip. There was also a small groove on the right side which was not altered. "Now," she says, "you can't keep me out of things. I can enjoy life like others."

playmate. There is no attempt on the part of a child to conceal his curiosity or to refrain from remarking about the defect publicly or from ridiculing the afflicted companion. Whether his intentions are malicious or sympathetic, he will be openly frank in his discussions and opinions. In a less purposeful manner he will shun the deformed associate or will force him into an inferior social position. A note of permanence is often added to these childhood stigmas by "dubbing" the deformed child with a derogatory nickname which refers to his defect.

It is little wonder, then, that the great majority of deformed children quickly develop a feeling of inferiority and a sense of shame. Probably this mental factor develops much earlier than is generally realized.<sup>1</sup> We recall two infants about 2 years of age with harelip. One would manipulate his lip while looking into a mirror and the other would hide his mouth with a pillow when any one approached. This "inferiority complex" does not usually become a serious problem until the child enters school. He is then brought to realize his difference from the others and finds that he is not able to acquire the intimate companionships enjoyed by his playmates. As the child matures he becomes increasingly more sensitive. When adolescence is reached a sense of despair and a pessimistic philosophy of life admixed with all sorts of peculiar personality traits have been established.

2. *Modifications of Self Expression.*—Lowrey<sup>2</sup> tells us that personality depends on two fundamental drives. The one is for self expression and the other for conformance with accepted social standards. When these two factors coincide, a pleasing personality develops.

When this is applied to the deformed child, the result is obvious. The deformed child may have every mental and physical faculty for self expression possessed by other children but, because of his deformity, he is either restrained by others or avoids the personal contacts necessary for such expression. Activities are either shunned or altered.

Three reactions may result: First, the child may succumb to these obstacles and accept non-expression as his lot. Second, the child may develop a compensatory overabundance of self expression to satisfy his injured ego. Third, under fortunate circumstances the deformed child may replace the suppressed modes of self expression with alternative ones of equal merit.

3. *Antisocial Tendencies.*—A second important factor in the development of personality is the acquisition of popularity. Before a handicapped child can gain recognition of the group he must first overcome the tendency of other children to maintain the natural impression of abnormality and undesirability. Many unfortunates are inclined to give in to these difficulties and to make no effort to become one of the group. Others become resentful toward their obstacles and mistreatment. Blame for their failures is either inwardly or openly placed on all manner of circumstances and people. From the sociologic point of view, this is the dangerous group. These are the children who may develop distinctly objectionable social behavior, since they often cannot obtain desirable employment, may not succeed in matrimonial ventures and will not maintain friendships. As a result, they may resort to criminal activities. Evans<sup>3</sup> has given an excellent fictitious description of a boy who was taunted and ridiculed with the nickname "Barracuda" because of his ugly protruding teeth. This boy's retaliation was to make good his nickname, becoming a relentless criminal. The author suggests "Thus do the cruelties of youth create rogues."

The rarely spontaneous reaction occurs when the handicapped child sets out to make himself popular



Fig. 2.—A, cleft palate in the same girl shown in figure 1. B, appearance of palate after correction. Palates should be repaired when the patient is 2 years of age to prevent serious speech impediments, which cause untold embarrassment. They can, however, be operated on at any age with great improvement of speech tone, as in this case.

regardless of obstacles. This is a goal toward which mental therapy should be aimed when dealing with handicapped children.

#### SURGICAL CARE OF DEFORMITIES

1. *Prevention.*—Very little is known about the prevention of congenital deformities. Acquired deformities, on the other hand, are largely preventable through

1. Straith, C. L.: Plastic Surgery: Its Psychological Aspects, J. Michigan M. Soc. 31: 13-18 (Jan.) 1932.

2. Lowrey, L. G.: The Effects of Physical Handicaps on Personality, Hosp. Soc. Serv. 13: 237-241 (March) 1926.

3. Evans, E. R. G., R.: Ghosts of the Scarlet Fleet, New York, Farrar and Rinehart, 1931.



safety measures. However, once an injury capable of producing a deformity has been inflicted, the preventive measures employed are entirely dependent on the resources of the physician responsible for its care.

Accidental injuries to the face lead the list of acquired deformities.<sup>4</sup> The management of every injury to the soft tissue of the face requires painstaking care and often demands a slow meticulous repair. Prolonged general anesthesia is often needed to insure the operator's

affected with one or two layers of minute subcuticular sutures<sup>5</sup> (fig. 6). Coarse sutures and skin clips cannot be too heartily condemned, since the resulting irregularities and stitch marks constitute deformities in themselves. If interrupted sutures must be resorted to (as around sharply curved lacerations) they should be of fine horsehair in which only the first double twist of a surgeon's knot has been tied—never completed to form a square knot. This permits accurate approximation but allows some expansion to compensate for edema. Surgical incisions on the face should be similarly treated and, in addition, should be planned to follow Langer's lines of skin elasticity. Bony injuries of the face are specialized problems, the discussion of which is too extensive for this paper. Those who are not familiar with their management are referred to more detailed publications.<sup>6</sup> Let it suffice to mention the difficulties in

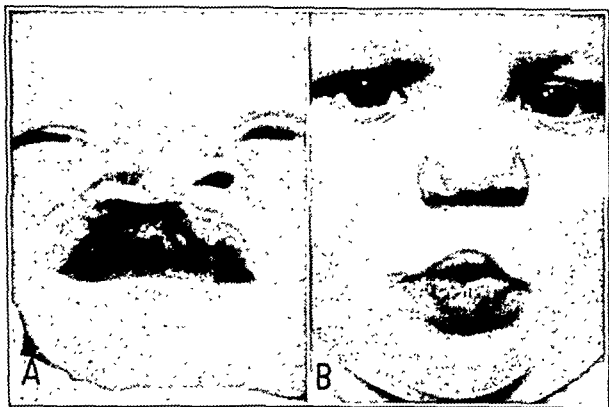


Fig. 3.—A, wide single harelip in a newborn infant. Note the flatness of the right ala with distortion of the nasal tip and the wide cleft of the alveolar ridge, through which the tongue can be seen. B, appearance after repair. Harelips should be corrected during the first few days of life under local anesthesia. A few drops of procaine hydrochloride in each infra-orbital foramen and at the base of the nasal septum will suffice. The shock to the child is negligible and the relief to the parents immeasurable.

unhindered freedom to do careful work. The simplest brush burns should be carefully scrubbed with soap and a soft brush to reduce the danger of tattoo marks of oil or dirt (fig. 5). Embedded cinders or grains of dirt must be plucked out one by one. In deeper wounds, all nonviable tissue should be carefully debrided. Small fragments of bone or cartilage, on the other hand, should seldom be removed. These apparently useless bits rarely sequester and are most necessary to maintain the normal contours of the face. Beveled or ragged



Fig. 5.—Bluish oil and cinder tattoo marks resulting from dirty abrasions acquired several months previously. Such deformities are very common among children who are victims of accidents in the street. At the time of emergency treatment this type of disfigurement can often be minimized by thorough scrubbing, under anesthesia, with soap and a soft brush. Satisfactory correction at a later date is almost impossible with such extensive tattooing as this case presents.

early diagnosis of bony lesions. The presence of excessive edema and the absence of severe pain usually hide the existing injury. This is especially true of nasal fractures but applies also to those of the frontal bone, malars, maxilla or mandible. Every injury to the face, however innocent in appearance, should be carefully checked by inspection, palpation and x-ray examination for possible fractures.

Preventive aspects of the care of burns have been more widely publicized. The use of tannic acid should be a matter of routine. The earliest possible skin grafting of burns should also be a familiar sequence. One suggestion might be made about the prevention of con-

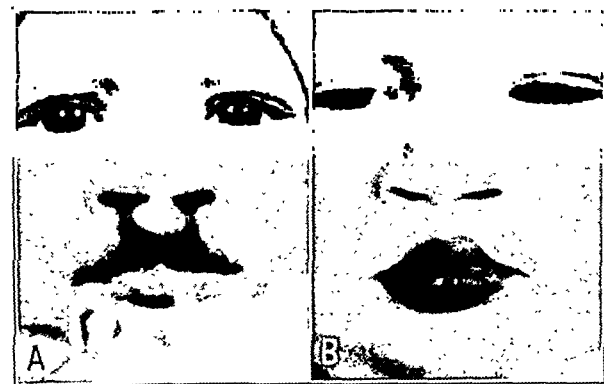


Fig. 4.—A, double harelip in a newborn infant. Note the absence of a columella, leaving the midportion of the lip attached directly to the nasal tip. This is an almost universal occurrence in double harelip. B, correction made by Federspiel method. This procedure usually gives a "cupid's bow" shape to the vermilion border, as seen in this case. We prefer to reconstruct the columella at a later date, using all available tissue for the lip at the first operation.

wounds should be carefully straightened and undermined. All lacerations should be approximated with numerous buried white silk sutures and further per-

4. Straith, C. L.: Automobile Injuries, *J. A. M. A.* 109:940-945 (Sept. 18) 1937; Management of Facial Injuries Caused by Motor Accidents, *ibid.* 108:101-105 (Jan. 9) 1937.

5. Straith, C. L.: Facial Scars, *Am. J. Surg.* 36:88-90 (April) 1937.  
6. Blair, V. P., and Ivy, R. H.: *Essentials of Oral Surgery*, St. Louis, C. V. Mosby Company, 1936. Straith, C. L., and De Kleine, E. H.: Modern Management of the Fractured Nose, *Internat. Abst. Surg., Gynec. & Obst.* 66:9-15 (Jan.) 1938. Straith.<sup>4</sup>

tractures: As soon as the immediate shock of the burn has passed, all burned flexor surfaces should be placed in full hyperextension and kept in this position for a prolonged period. This involves considerable ingenuity with splints and traction but will minimize almost every contracture resulting from a burn (figs. 7 and 8).

**2. Earliest Possible Correction.**—When a deformity of any type or severity is present the most important single item in the avoidance of undesirable personality changes is the most complete surgical restoration possible at the earliest date that is feasible. This is a hard and fast rule with no exceptions of which we are aware.

Although this may seem obvious, there are nevertheless many parents who are not so advised. The reason is twofold. First, the average physician sees such cases seldom and hence is not informed on the technical aspects of therapy. Second, plastic surgery has undergone such great advances since the World War that the information contained even in standard textbooks of surgery is often obsolete and misleading.

It is of particular importance to have deformities corrected, if possible, before the child enters school. This is the age of greatest mental and social reaction to deformity, from which every effort should be made to

not to be overlooked, is the happiness of parents, who by an early operation are spared months of heartache and embarrassment.

We feel that cleft palates should not be operated on before the child is from 18 to 24 months of age (fig. 2). Earlier than this the palatal tissue is too flimsy to permit adequate repair without tearing. Prevention of speech defects is the paramount aim, and, since most children begin to talk at about 2 years of age, this is the age of

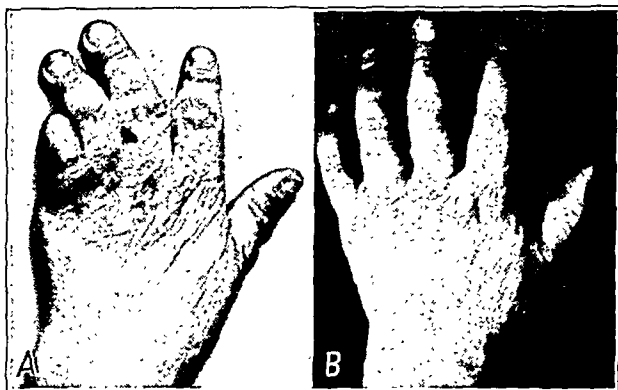


Fig. 7.—A, webbing of the fingers and contracture of the little finger from hot water burns. This 4 year old boy was very much concerned about his deformity and would not tolerate any ridicule from his playmates. Because of excellent home training, he developed a great interest in the correction of his deformity and maintained a pleasing personality in spite of his handicap and the necessity for considerable surgery. B, same after correction with Wolfe grafts from the thigh. The procedure used here to separate the fingers is identical with that used for congenital webbing. Massage and exercise will improve the usefulness of this hand still further.

choice for surgery of the cleft palate. Even after a satisfactory anatomic repair, speech training with hours of patient practice is required to insure a satisfactory speaking voice. In certain cases in which there is difficulty due to shortness of the palate, the Dorrance "push-back" operation may be performed to give the palate its needed length.<sup>7</sup>

Plastic surgery involving the legs or abdomen must usually be delayed until the child passes the diaper age



Fig. 6.—A, extensive facial lacerations resulting from automobile accident. Both inner canthal ligaments were divided and the nasal bones were broken away from the nasal process of the frontal bone. B, canthal ligaments were reattached by suturing them together through the nose. Nasal bones were wired to the frontal bone through small drill holes in each. Lacerations were carefully approximated with subcuticular suturing. Note the almost complete absence of visible deformity after healing. We advise more careful attention to all facial wounds and suturing in such a way that stitch marks and scarring are reduced to a minimum. The use of coarse sutures and skin clips cannot be too heartily condemned.

protect the child. Fortunately, there are but few conditions in which at least partial restoration cannot be made during the first five years of life.

**3. Management of Common Deformities.**—Among the congenital deformities there is a group which allows correction immediately after birth. Most conspicuous of these are the harelips (figs. 1, 3 and 4). In the absence of specific contraindications to surgery, harelip should be corrected during the first week of life. With paregoric for premedication, this repair can be safely and efficiently performed with a simple nerve block anesthesia. We have performed such surgery within twenty-four hours after birth, often with the child sleeping through the operation. The advantage of such early intervention is primarily that the earlier the repair the better the return of both the lip and the bony framework to their normal configuration. This is especially true when there is a cleft of the alveolar ridge. With but few exceptions early repair of the lip results in a spontaneous closure of the alveolar cleft. Second, the younger the infant the more satisfactory the local anesthesia with its added safety. A third indication, one



Fig. 8.—A, contracture of the axilla resulting from a burn. This girl also had extensive contractures of the chest and groin, which were relieved by the insertion of large Thiersch grafts. B, same girl after correction with a Z plasty to bring extra skin into the line of contracture. Note that the surgical scars lie across the axilla rather than longitudinally. This prevents recurrence due to shrinkage of the scar tissue.

because of the danger of infection. This includes the use of skin or fascial grafts taken from the lower part of the abdomen and the upper part of the thighs (figs. 7 and 11).

7. Dorrance, G. M.: *The Operative Story of Cleft Palate*, Philadelphia, W. B. Saunders Company, 1933.

Lop ears are very common and very annoying deformities (figs 9 and 10). The use of corrective appliances or adhesive tape never reduces their prominence and should never be advised because of the false hope that it creates. Very marked lop ears should be corrected before school age to avoid the malicious torment

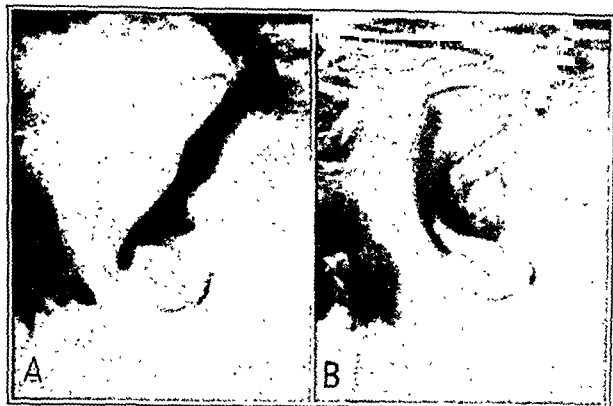


Fig. 9.—A, hideous lop ears in a young girl which caused her to be nicknamed "flop-ears." Her mother states in a letter: "With all her gumption, she never volunteered to do anything that would place her directly before an audience because of her hair being thin and her ears protruding. When she ran, her hair would fly over her face and, instinctively, her hands would fly up to her head and hide the ears." B, same patient after correction. The mother expresses our point of view when she writes: "I cannot speak or write too emphatically on the absolute advantage of operating on children's deformities before they become of school age. The biggest improvement is in R's disposition. She was always on the warpath if any one looked at her in a questionable manner. She is a much better sport and, consequently, has more girl friends. She used to play with boys almost exclusively because it seemed that they didn't notice her ears, or if they did they rarely commented on them like the girls did. She takes more pride in her appearance. The operation has given her a certain sense of equality with the rest of the little girls."

of derogatory nicknames and teasing. Correction of the less marked varieties depends on the attention they excite in playmates and the child's self consciousness of the abnormality.

Nasal deformities do not usually make their appearance until adolescence (figs. 12, 13, and 14). Hump nose, saddle nose and even the traumatic nasal deformities often do not become apparent until this age, when

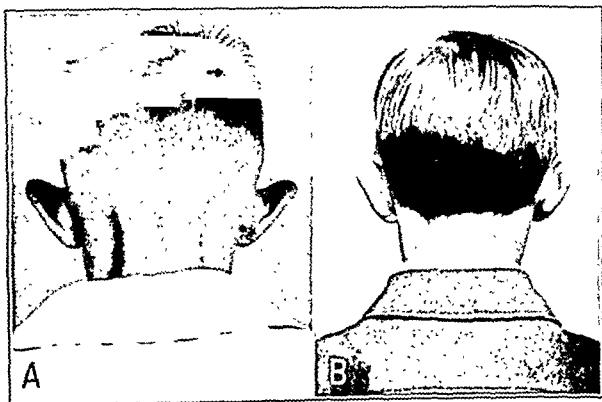


Fig. 10.—A, lop ears in a boy. Boys are more frequently troubled by this deformity than girls because of the shorter haircuts. Unless corrected before school age, even minor protrusions give rise to great distress and derogatory nicknames such as "jug-handle" or "mule-ears." B, same patient after correction. An elliptic area of skin is removed from the back of the ear and the scalp. The necessary amount of cartilage is then removed so that the ears will remain at about a 45 degree angle from the mastoid. Adhesive strapping will not reduce the degree of protrusion and is a waste of time for both physicians and parents.

ossification of the nasal bones is complete. During this period the nose is continually changing shape. Many plastic surgeons prefer to delay nasal plastic operations until after these changes are complete, but it is our

opinion that marked deformities, or even minor ones that are causing personality changes, should be corrected in the early teens. At this age children develop an exaggerated impression of personal appearance. Self consciousness flourishes as at no other time in life. It is therefore our policy, if at all feasible, to correct major nasal deformities at this time, even though it may be necessary in some cases to do a secondary plastic operation after the nose has more fully acquired its mature characteristics. Until recently it has been impossible to correct childhood saddle noses with cartilage grafts because of the immaturity and softness of a child's rib cartilage. It is now possible to use preserved adult cartilage and to replace or add to this cartilage at a later date if necessitated by further development of the nose.<sup>8</sup> A minor secondary operation seems insignificant in comparison to the drastic personality changes that often result from self consciousness engendered by a deformity.

We have already mentioned the procedures which should be employed immediately after injury to prevent traumatic disfigurement. If for any reason a deformity of the soft tissue results, the corrective plastic pro-



Fig. 11.—A, congenital ptosis of both upper lids. Note the characteristic backward tilt of the head, to facilitate horizontal vision, and the tendency to let the lower jaw drop. B, same patient after correction by construction of fascial tendons from the tarsus to the frontalis muscle. The father says: "To us, he does not even appear to be the same child that he was before the affliction was remedied. We feel that we have saved him many hours of suffering from ridicule by his schoolmates had his condition been allowed to remain. Even as young as he is (8 years), A. has told us many times that he is glad we had the operation performed and that he looks like the other boys."

cedures must usually be delayed until about three months after healing is complete. This is to allow for complete disappearance of latent bacterial contamination, which is almost invariably present. Even the slightest or most localized recurrence of infection diminishes the perfection of a plastic repair. Bony injuries, on the other hand, allow an attempt at correction any time up to two or three weeks. During this time the possibility of repositioning the fragments by breaking up fibrous union gives greater hope of a satisfactory result than any subsequent reconstructive operations.

#### DEVELOPMENT OF SOUND MENTAL HEALTH

Surgical correction in early childhood is the most valuable method of preventing undesirable personality traits. Unfortunately, early correction of the deformity in some instances is impossible; in others it is impossible to obtain a perfect cosmetic result. Therapy, therefore,

8. Pierce, George Warren, and O'Connor, Gerald Brown: *Reconstructive Surgery of the Nose*, Ann. Otol., Rhin. & Laryng. 47: 437 (June) 1938.

must often be supplemented by special training to prepare the child for his handicap. This so-called "special" training is really not special in any sense of the word. It is the same training that might be recommended for any normal child, with emphasis on certain aspects which are most important to the deformed child.

1. *Courage to "Face the Facts."*—First, the deformed child must learn to anticipate difficulties and to be self reliant. Every effort should be directed toward not allowing the child to be spoiled. This training must begin as soon as the child is born by not responding with a burst of attention every time the baby cries or frets or bumps his head; as the child grows older, the same principles should continue in application. It is impossible to enumerate the method of handling each and every situation as it arises.

Since the deformed child is probably destined for one or many operations with some degree of pain, he should be thoroughly prepared for this ordeal. He should not be cajoled into the physician's office dishonestly by being told that it will not hurt or that the "boogerman" will get him if he doesn't go, or by being told that he is "going down town to get a soda." He should be given

dren's Center has shown us records of a boy with badly disfiguring facial burn scars who stole money for candy to pass around, probably for the same reason. He had been nicknamed "scarface," many children even being afraid to hold his hand in games at school. They also showed us the history of a boy with maladjustment fol-



Fig. 12.—*A*, marked hump nose with overhanging nasal tip in a young girl. We are told that she did not get along well with other girls since she was always under a delusion that she was being picked on because of her appearance. *B*, same patient after correction by modification of Joseph's technic. This alteration in appearance has done a great deal to stabilize her emotional difficulties and to improve her social conduct. The correction of conspicuous nasal deformities at early high school age will make the lives of such girls much happier.

to understand that he may be hurt and should at all times be told by both the physician and his parents exactly what to expect. We have seen children of very tender years who were so concerned about the correction of their deformities that several operations and months of treatment have failed to excite a tear; and we have seen older children howl profanely with anger at the removal of a stitch—both undoubtedly conditioned by their training.

2. *Interpretation of Values.*—The handicapped child is most likely to be deprived of many things commonly sought after for their supposed value; for example, money, friends, esteem, beauty, amusements and romance. Unless such children realize that regardless of group standards in this respect true value depends entirely on the enjoyment they themselves derive, they are apt to do many useless, foolhardy or even dishonest things to attain their desires, especially for friendship. Lowrey<sup>2</sup> describes a handicapped boy with a long history of petty pilfering for the purpose of having money to attract companionships. The Detroit Chil-



Fig. 13.—*A*, saddle nose resulting from a childhood fracture, giving this boy a pugilistic appearance. Athletic injury in childhood is one of the commonest causes of this deformity. At the teen age, personal appearance means a great deal to these children and complexes often result from the self consciousness produced by such a deformity. *B*, after correction with cartilage grafts. Formerly, correction of this defect was impossible owing to the softness of a child's rib cartilage. Now the deformity can be remedied with preserved adult cartilage, as in this case.

lowing a severe burn with prolonged hospitalization who gave his toys away to other children. Judge Healy states that "buying their way" is a common origin of criminal activities in handicapped children.<sup>9</sup>

Parents of such a child should make every effort to help him readjust his sense of values. Above all, he must learn that true friendship exists only in those who like him in spite of his deformity and irrespective of his possessions or ability to do something to "buy" their favor.

3. *Compensatory Education.*—We have already discussed the importance of speech training for children



Fig. 14.—*A*, saddle nose resulting from a blow with a baseball bat. Note the broad flat appearance of such a defect. *B*, correction with two pieces of rib cartilage, one to support and narrow the bridge and one as a strut to raise and narrow the tip. This girl's high school life has been made infinitely happier because of this reconstruction.

with cleft palate and we have indicated that such education is almost as important as the surgical repair. Physical therapy and gymnastics are important for children with orthopedic deformities, and contractures from burns, after correction, frequently require muscu-

9. Deneek, H. L.: Crippled Personalities, *The Crippled Child* 15: 130-133 (Feb.) 1938.

lar rehabilitation. We are told by ophthalmologists that crossed eyes are greatly improved by exercises to develop the use of extra-ocular muscles.

The important phase of compensatory education for most deformed children is that directed toward feasible modes of self expression and, later in life, toward trades and professions which will not be hindered by the deformity. To be successful, this training must follow the child's own interests and talents and should never be forced or predetermined by parents or teachers. Constructive hobbies and employment which keep the child happily occupied in his spare time are of the greatest value. Special training in art, music, athletics, handicrafts and the like should be made available wherever possible.

Whatever type of compensatory education can be worked out, if the child finds one or more satisfying methods of self expression which keep him happily occupied and which receive recognition from others, that child will probably develop along essentially normal lines, regardless of his deformity.

#### SUMMARY

1. The problem of deformities in children is a very serious one which has failed to attract adequate attention within the medical profession. The importance of deformities lies in the severe mental reactions and alterations of personality which result.

2. Many of the acquired deformities are preventable and all can be minimized by more careful attention to injuries and burns in visible areas of the body, especially the face. The technical information regarding this phase of preventive medicine should be more widely publicized among medical schools and medical organizations.

3. In the presence of deformity, the most important single factor in the avoidance of undesirable personality changes is the most complete surgical restoration possible at the earliest date that is feasible. Wherever possible, childhood deformities should be corrected before the child reaches school age, and a few are best corrected within the first week of life.

4. Many childhood deformities have become amenable to plastic surgery with the development of that specialty which has taken place since the World War. Still other deformities can be corrected by orthopedists, dentists, ophthalmologists or dermatologists.

5. In addition to surgical care, deformed children require more than ordinary "bringing up" at home and at school. They must be prepared to face greater hardships than normal persons and should be given special training to compensate for altered facilities for self expression.

1713 David Whitney Building.

**Every Soldier Was Given a Lemon a Day.**—Since ancient times scurvy has often been a scourge of armies in war time. As is well known, the disease is due to the diet being deficient in vitamin C. The patient feels tired, has pains in the joints, the gums swell and bleed. Later the skin becomes covered with petechiae and hemorrhages occur. The soldier can no longer march and is useless. Scurvy was rampant in the Abyssinian army on the Somaliland front. From reports of foreign doctors in the Ethiopian Red Cross, they had over 30,000 cases. There were no cases in the Italian army. What was the reason? A small precaution: every soldier was given a lemon a day.—Castellani, Sir Aldo: Hygienic Measures and Hospital Organization of the Italian Expeditionary Forces During the Ethiopian War, 1935-1936, *J. Roy. Nav. M. Serv.* 24:304 (Oct.) 1938.

## TUMORS OF THE FOURTH VENTRICLE

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The early diagnosis of tumors of the fourth ventricle makes possible a more complete removal of the tumor, greater relief of symptoms, and a lowered operative mortality. Early diagnosis is difficult because tumors of the fourth ventricle produce symptoms of increased intracranial pressure. Our cases in which operation was performed have been reviewed in an effort to emphasize any factors which may help in recognizing the early symptoms and determining the treatment.

There have been very few reviews of tumors of the fourth ventricle in which large series of cases have been analyzed. In the more recent textbooks of neurology, such as those by Wechsler,<sup>1</sup> Grinker<sup>2</sup> or Stewart,<sup>3</sup> the consensus is that tumors of the fourth ventricle produce general symptoms of increased intracranial pressure by obstructing the circulation of cerebrospinal fluid. It is only in the later stages of the growth of the neoplasm that signs referable to the cerebellum, medulla oblongata

Medulloblastomas	31	██████████
Ependymomas	21	██████████
Astrocytomas	19	██████████
Oligodendrogliomas	4	████
Hemangio- endotheliomas	3	███
Gliomas of granular layer	2	██
Epidermoid cyst	1	█
Papilloma	1	█
Total	82	████████████████████

Fig. 1.—Relative frequency of the different types of tumors of the fourth ventricle.

or pons may be elicited. Parker<sup>4</sup> drew attention to the periodicity of symptoms which some tumors of the fourth ventricle produce. He also discussed the frequency with which some tumors of the fourth ventricle produce sudden death.

#### REVIEW OF CASES

Eighty-two cases have been included in this review and only the predominant universal symptoms have been listed. In this survey we found that frontal or occipital headache, nonprojectile vomiting, ataxia, visual disturbances including diplopia and nystagmus, and the usual symptoms of intracranial hypertension were the outstanding clinical characteristics. The most successful surgical results were obtained in the cases in which a diagnosis had been made early and removal of the tumor had been effected before there had been any irreparable injury of the brain.

In our series of eighty-two cases (fig. 1) there were thirty-one medulloblastomas, twenty-one ependymomas,

From the Section on Neurologic Surgery (Dr. Craig) and the Section on Neuropathology (Dr. Kernohan), the Mayo Clinic. Owing to lack of space, this article has been abbreviated for publication in THE JOURNAL. The complete article appears in the authors' reprints.

Read before the Section on Nervous and Mental Diseases at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.

1. Wechsler, I. S.: A Textbook of Clinical Neurology, ed. 1, Philadelphia and London, W. B. Saunders Company, 1931.

2. Grinker, R. R.: Neurology, Springfield, Ill., C. C. Thomas, 1934.

3. Stewart, J. P.: The Diagnosis of Nervous Diseases, London, Edward Arnold & Co., 1931.

4. Parker, H. L.: Tumors Involving the Fourth Ventricle of the Brain, Thesis, 1923.

four oligodendrogliomas, two gliomas of the granular layer of the cerebellum, one epidermoid cyst, three hemangio-endotheliomas, nineteen astrocytomas and one papilloma of the choroid plexus. There was nothing particularly characteristic about the ages of the patients except perhaps in the cases of hemangio-endothelioma, in which the oldest patient was 45 years of age and the youngest patient 17. The rest of the patients were between 2 and 34 years of age.

In seventy-nine of the eighty-two cases, headache was one of the initial symptoms (fig. 2). In thirty-four cases the headache was in the frontal region and in thirty-nine cases it was in the occipital region. In sixty-seven cases vomiting also was one of the initial symptoms; in nineteen cases it was projectile and in forty-eight cases it was nonprojectile. One of the commonest neurologic manifestations was ataxia; in sixty-four cases the ataxia occurred relatively early in the history of the disease. Visual difficulty was a common symptom; thirty-one patients complained of visual impairment and fifty-five complained of diplopia. Hiccup has been a rather predominant symptom in cases reported in the literature but this symptom occurred in only eight of our eighty-two cases. Thirty-four of our patients had a stiff neck. Nystagmus was present in sixty-one cases and a choked disk was found in seventy-four cases. It was rather interesting to know that previous to operation it was necessary to make ventriculograms in only twenty-four cases. In the rest of the cases the localization was so definite that ventriculograms were not necessary. In sixty-two of the cases only part of the tumor was removed but in twenty cases the entire tumor was removed. As one reviews the histories one is struck with the fact that the entire tumor could have been removed in a larger number of cases if relief had been sought earlier in the course of the disease. In most of the cases in which the entire tumor was removed the history indicated that the tumor had been present only a short time. It is also interesting to note that of the thirty-one medulloblastomas thirty were removed partially and one was removed entirely. Of the twenty-one ependymomas thirteen were removed partially and eight were removed entirely. Of the entire group of astrocytomas only four were removed entirely.

The survival period in the cases of medulloblastoma did not seem to depend on the amount of tumor which was removed or on the amount of high voltage roentgen therapy given but on the type of cells found. For example, in one case of medulloblastoma in which microscopic examination of the tumor revealed a large number of astrocytes the patient, who was 34 years of age, lived five years after subtotal removal of the tumor. She was returning to the clinic to undergo a second operation when she died suddenly. In the majority of cases of medulloblastoma the period of survival is from nine months to three years; in cases of ependymoma, however, the life expectancy is much longer, even in cases in which only part of the tumor is removed. One patient with ependymoma lived for eleven years following subtotal removal, before it was necessary to perform a secondary operation. Of the four patients with oligodendroglioma, three lived for from three to four years following operation. One man with hemangio-endothelioma is alive six years and one woman is alive five years after operation.

In reviewing our series of cases it has been noted that during the earlier years of neurosurgery as much

of the tumor as possible was removed at operation, regardless of the type of glioma, and roentgen therapy was used regardless of the type of tumor, while in later years, when we were able to distinguish the ependymomas and the medulloblastomas, the operative procedure varied. It also is interesting to note that during the past few years, after we had become more proficient in the diagnosis of fresh sections of the different types of tumor of the fourth ventricle, we have been more prone to carry out total removal, especially of the ependymomas and the astrocytomas, whereas in cases of medulloblastoma as much of the tumor as possible is removed but the radiosensitivity of the cells makes a radical resection less imperative.

#### PATHOLOGY

It generally has been thought that tumors of the fourth ventricle are more malignant than are gliomas that are found elsewhere in the central nervous system. This may be, and undoubtedly is, true from the clinical and surgical points of view, but cytologically it is not so.

Papillomas of the choroid plexus are rare neoplasms, but they usually grow slowly and can be removed. However, because of their situation in the course of the cerebrospinal fluid they may be implanted elsewhere in the subarachnoid spaces, as described by Hall and

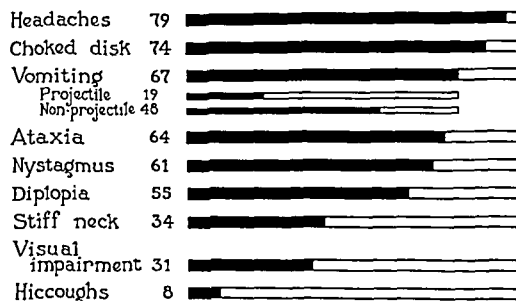


Fig. 2.—Predominant symptoms in eighty-two cases of tumor of the fourth ventricle.

Fentress.<sup>5</sup> Ependymomas that arise from the wall of the fourth ventricle are more common, and we have observed twenty-one cases (not including cases in which operation was not performed) of this type of glioma. As a rule, these tumors grow slowly and lend themselves to surgical removal. In several previous studies we have subdivided ependymomas into three types. The epithelial type contains canals or cavities that are lined with ependymal cells. These ependymal cells simulate epithelial cells. There is another type of growth in which the ependymal cells assume a papillomatous appearance and grow around a core of connective tissue. The stroma frequently undergoes myxomatous degeneration. We have termed this subdivision the "myxopapillary type." There is a large group of ependymomas in which the cells assume no characteristic arrangement and because of its cellular appearance we have termed it a "cellular type of ependymoma." This term is somewhat misleading because cellularity in a general way indicates malignancy, but this group of ependymomas is not necessarily more malignant than the other subtypes. Less than 5 per cent of ependymomas are highly malignant and tend to recur rapidly; however, these malignant ependymomas respond rather readily to roentgen therapy.

5. Hall, G. W., and Fentress, T. L.: Papilloma Choroideum with Diffuse Central Nervous System Metastases, *J. Neurol. & Psychopath.* 14: 108-115 (Oct.) 1933.



Astrocytomas are rather commonly found arising from the tissues around the fourth ventricle. They do not differ histologically in any respect from astrocytomas found elsewhere in the central nervous system. Cushing<sup>6</sup> studied and described seventy-six astrocytomas that occurred in the neighborhood of the fourth ventricle; no further discussion of this type of tumor is necessary as we cannot add anything to his excellent description.

Hemangio-endotheliomas have been found in all parts of the central nervous system, but they are more

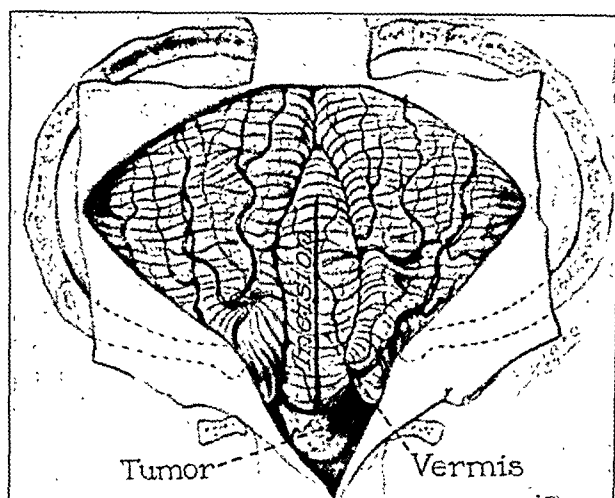


Fig. 3.—Tumor of the fourth ventricle presenting below the vermis and the line of incision of the vermis necessary for adequate exposure.

common in the cerebellum than they are elsewhere. These tumors may be associated with hemangiomas of the retina, telangiectasis of the skin, cysts of the pancreas, liver, kidneys or spleen; this syndrome frequently is referred to as Lindau's disease. A hemangio-endothelioma of the cerebellum is usually a small nodule on the wall of a large cyst in the cerebellum; the cyst is usually the result of an exudate from the vascular tumor. This type of tumor is commonly hereditary and is thus of eugenic importance. Hemangiomas unassociated with the formation of cysts or lesions elsewhere in the body do occur in the cerebellum and fourth ventricle.

It is probably true that medulloblastomas which usually arise in the vermis of the cerebellum of children should be included in the group of highly malignant gliomas. We have studied thirty-one medulloblastomas. These tumors have a tendency to implant themselves on the walls of the other ventricles and to be disseminated widely throughout the subarachnoid space. This fact should be kept in mind when roentgen therapy is undertaken for their relief. Medulloblastomas are supposed to respond better to roentgen therapy than other types of glioma. This is another reason why it is important to distinguish histologically between the various types of gliomas found in and around the fourth ventricle; it is impossible to distinguish the various types either clinically or by gross inspection. The extent of surgical removal and the subsequent treatment and prognosis depend to a large extent on the type of glioma found on microscopic study.

6. Cushing, Harvey: Experiences with Cerebellar Medulloblastomas: A Critical Review, *Acta path. et microbiol. Scandinav.* 7: 1-86, 1930; Experiences with Cerebellar Astrocytomas: A Critical Review of Seventy-Six Cases, *Surg., Gynec. & Obst.* 52: 129-204 (Feb.) 1931.

# SURGERY

Operation for the removal of a tumor of the fourth ventricle can be conducted with the patient in the upright or prone position. In most cases the upright position allows for a drier operative field and permits better exposure of the fourth ventricle. If the upright position is used, signs of changes in or instability of the blood pressure rarely develop. We have found that blood transfusion or the intravenous administration of physiologic solution of sodium chloride and dextrose during the operation help to reduce the incidence of instability of the blood pressure. In the upright position the operation can be carried out under either local or general anesthesia. We have found it more advantageous to use ether administered by the intratracheal method or to use a combination of intratracheal anesthesia and local infiltration. The Cushing cross-bow incision has been replaced almost invariably by a simple curved incision which is started below the mastoid process on each side and curved upward to just below the occipital protuberance. Sufficient exposure is thus obtained to remove the bone over both cerebellar lobes, the arch of the foramen magnum and the arch of the first cervical vertebra or atlas. Usually the inferior tonsils of both cerebellar lobes are herniated below the level of the foramen magnum and in a certain number of cases one can observe the lower margin of the tumor below the vermis. In order to obtain adequate exposure of the tumor sometimes it is necessary to divide the vermis (fig. 3). On the other hand, when the vermis and the inferior tonsils of the cerebellum are not herniated it is sometimes possible to remove the entire tumor without incising the vermis. It usually is necessary to aspirate the posterior horn of the lateral ventricle before opening the dura. After the tumor of the fourth ventricle has been removed, air can be injected into the posterior horn of the lateral ventricle; when the air bubbles through into the fourth ventricle it demonstrates that the aqueduct of Sylvius is patent (fig. 4). This is much safer than

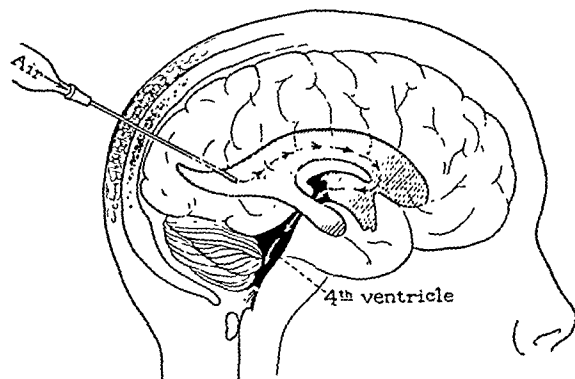


Fig. 4.—Test for patency of the aqueduct of Sylvius and fourth ventricle following removal of a tumor.

attempting to pass a catheter into the aqueduct, as the latter procedure may produce trauma. Postoperative drainage is sometimes advantageous and can be accomplished by either leaving a catheter in the posterior horn of the lateral ventricle or by placing a small collapsible Penrose drain in the fourth ventricle. Postoperative drainage performs several functions. Regardless of the care with which the closure is made there frequently is a small amount of residual blood in the wound. A Penrose drain can safely be inserted through a stab wound in the center of the flap; it is allowed to

remain in place for twenty-four hours and allows the drainage of cerebrospinal fluid to wash all the blood from the posterior cistern. This obviates the necessity for the absorption of blood and also minimizes the tendency to the development of adhesions. We have now been using drainage in these cases for several years and we have found that it lessens the tendency of a postoperative increase of temperature, the formation of cysts and delayed absorption of the fluid around the posterior cistern. Since the advent of the electro-surgical unit we have used it with success in the treatment of all types of intracranial tumors. However, we have also found that the use of the electric cautery around the floor of the fourth ventricle is sometimes followed by a severe reaction; therefore, removal of tumors of the fourth ventricle is carried out with suction and grasping forceps, and we have found that with care in controlling the hemorrhage very little electrocoagulation is necessary.

#### ADVANTAGES OF EXAMINATION OF FRESH FROZEN SECTIONS DURING OPERATION

Prior to the appearance of the monograph of Bailey and Cushing,<sup>7</sup> in which gliomas were classified histologically into their various subgroups, pathologists and surgeons were satisfied with the diagnosis of a glioma. All these neoplasms were treated alike but it was noted that they varied remarkably in the rapidity of recurrence after partial or even seemingly complete removal. Today the classification of Bailey and Cushing is generally accepted, especially by neurosurgeons. Most pathologists, given adequate time in which to apply special staining methods and to study various sections, can arrive at a correct classification of a glioma which the neurosurgeon has removed. This is important as it helps the surgeon in discussing the prognosis with the relatives of the patient and enables him to anticipate the help that can be expected from roentgen therapy. However, this does not help him in deciding how much of the neoplasm he should attempt to remove at operation. At the clinic the surgeons in general have been taught to, and now do, expect accurate diagnosis by examination of frozen sections of fresh tissue which have been removed for biopsy and they plan their surgical procedures accordingly. Wilson<sup>8</sup> developed this field of surgical pathology about thirty years ago, and since that time MacCarty, Broders and their co-workers have been using fresh frozen sections stained with polychrome methylene blue. In the field of neurosurgical pathology several workers have developed methods for the rapid diagnosis of gliomas. Eisenhardt<sup>9</sup> has successfully used neutral red as a vital stain for smears of gliomas and has described the various types of cells and their processes which are seen in gliomas. Russell<sup>10</sup> has used toluidine blue to stain smears of gliomas. The tissue is smeared on a microscopic slide and fixed rapidly, and the stain is applied. This method also demonstrated the various types of cells and their processes. We have been using polychrome methylene blue to stain frozen sections of fresh specimens of brain tumors for many years and have found it satisfactory. Aside from the fact that we have become used to this method, it seems

to us that it has the advantage of allowing us to study not only the individual cells but also the architecture of the neoplasm. We also can study the relation of the cells to the walls of blood vessels, changes in the blood vessels, especially proliferation of endothelial cells of the intima, and necrosis, mitotic figures and so on. The stain does not, as a rule, demonstrate all the processes of the cells, but diminishing the light which passes through the section makes it possible to visualize most processes. We keep most of our fresh frozen sections for several days, at least until the permanent sections have been made. This procedure allows us to compare the fresh sections with the fixed sections and is useful in teaching. The fresh sections are mounted in a 5 per cent solution of dextrose, and the edge of the cover glass is painted with "duco," which prevents evaporation of the aqueous solution that is

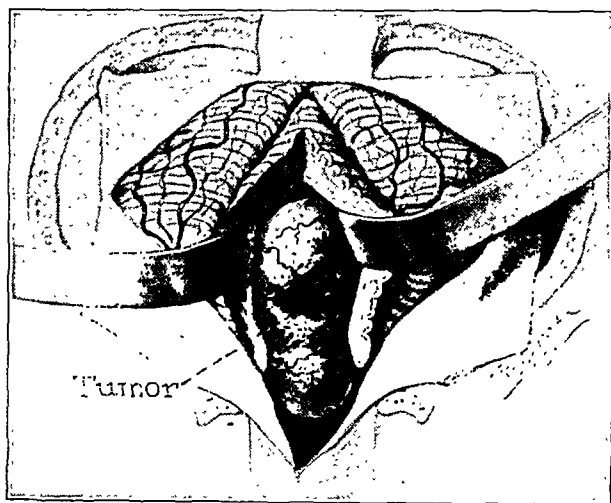


Fig. 5.—Hemangio-endothelioma exposed by dividing the vermis.

used for mounting. The sections may be preserved much longer if they are placed in a dark cold place.

The object of operation in cases of tumor of the fourth ventricle is to relieve the internal hydrocephalus or the increased intracranial pressure. Although a conservative operation which opens the lower portion of the aqueduct of Sylvius may be followed by temporary relief, if the surgeon is made aware of the malignancy of the tumor during the operation his method of attack and his attempt at radical removal are modified by the cytologic character of the tumor encountered.

#### REPORT OF CASES

CASE 1.—A man aged 49 came to the clinic complaining of headache, dizziness and failing vision. Frontal headaches had begun six months previously and a month later he had been seriously ill with influenza. Following this he had felt tired constantly, had had to force himself to work, and nearly every day he had had a mild frontal headache. The headaches had become extremely severe in the six weeks before his admission and he had had to stop work on account of dizziness. His vision gradually had become blurred and the headaches had become more severe. Examination revealed bilateral choked disks of 1 diopter in the right eye and 3 diopeters in the left eye. Neurologic examination revealed a slight increase of all reflexes on each side and some incoordination and ataxia. Ventriculography revealed bilateral internal hydrocephalus and dilatation of the third ventricle. During a suboccipital craniotomy the bone was found to be very thin and when the dura was incised a large reddish vascular tumor could be seen lying below the vermis, which was divided. A specimen of the tumor was removed for biopsy. Histologic examination of this speci-

7. Bailey, Percival, and Cushing, Harvey: A Classification of the Tumors of the Glioma Group on a Histogenic Basis with a Correlated Study of Prognosis, Philadelphia, J. B. Lippincott Company, 1926.

8. Wilson, L. B.: A Method for the Rapid Preparation of Fresh Tissues for the Microscope, J. A. M. A. 45: 1737 (Dec. 2) 1905.

9. Eisenhardt, Louise C.: Diagnosis of Intracranial Tumors by Supravital Technique: Further Studies, Arch. Neurol. & Psychiat. 28: 299-319 (Aug.) 1932.

10. Russell, Dorothy: Personal communication to the authors.

men, which was made during the operation, disclosed that the tumor was a typical hemangio-endothelioma. The growth was dissected from below upward; it was found to fill the fourth ventricle. Many large vessels entered the tumor from the cerebellum. These were ligated and Cargile membrane was packed about the tumor. It was necessary at this point to close the wound. The second stage of the operation was performed two weeks later, when the tumor was removed (fig. 5). After a rather stormy convalescence the patient returned home and was able to resume his duties as editor. When he was seen one year later his general condition was excellent, and two years later he was out making campaign speeches and working as hard as ever. It is now seven years since his operation and he is perfectly well.

Histologic examination revealed that the tumor contained numerous blood spaces, both large and small. The spaces were lined with endothelial cells; in some of the spaces the endothelial cells were swollen and cytoplasm was vacuolated; staining with sudan III disclosed that the vacuoles were filled with lipoids. In some regions the blood spaces were missing and there was an excess of loose connective tissue. However, there was no dense fibrous tissue or blood pigment. Perdrau's silver stain for connective tissue revealed that the reticulum radiated away from the larger blood spaces like the spokes of a wheel.

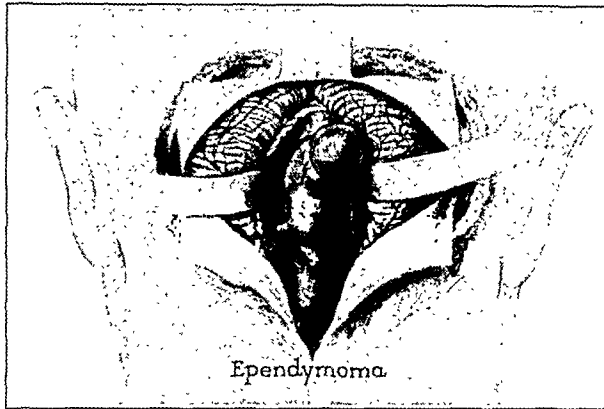


Fig. 6.—Ependymoma attached on the left side.

There were no evidences of hemangiomas of the skin or retina or of disease of the pancreas or kidneys, and there was no cyst associated with the tumor in the cerebellum; therefore we are not suggesting that this case is an example of Lindau's disease.

In the following case a tumor of the fourth ventricle was diagnosed early and removed entirely. Examination of fresh tissue during the operation disclosed that the tumor was an ependymoma. The postoperative course, which was thereby shortened, was uneventful.

CASE 2.—A girl aged 18 years was referred to the clinic because of headache, vomiting and pain in the neck. She had been perfectly well until ten months before she came to the clinic, when she had begun to have severe occipital headaches. The headaches had been mostly on the right side, had occurred at any time of the day and had lasted from two to three hours. They gradually had receded until they had occurred every two weeks, at which time they had awakened her in the morning. They had been associated with vomiting which had not been projectile or associated with nausea. Immediately after vomiting the headache had been relieved. Five months previous to her examination she had entered college and her vomiting had been attributed to hyperacidity, which had improved temporarily following the daily administration of alkalis and non-acid forming foods. Two weeks before she was examined at the clinic she had noted a dull pain in the back of the neck; the pain had been associated with the headaches. She had had one attack of hiccups. Examination disclosed a slight tremor of the eyelids and hands and tenderness on percussion of the occipital region of the skull. There was no bruit but the neck was slightly stiff. Examination of the eyes revealed that vision

was 6/10 in both eyes. Examination of the ocular fundi revealed a choked disk of 7 and 8 diopters in the right eye and a choked disk of 6 and 7 diopters in the left eye. Examination of the visual fields revealed enlarged blind spots in both eyes. Roentgenograms of the head revealed intracranial pressure and pressure erosion of the sella turcica. A suboccipital craniotomy revealed a tumor of the fourth ventricle. The tumor, which was granular and reddish, extended below the herniated inferior tonsils to the level of the second vertebra. Examination of frozen section, which was stained with polychrome methylene blue, revealed that the tumor was an ependymoma. This examination was made during the operation. The tumor, which was attached to the floor of the fourth ventricle on the left side, was removed completely (fig. 6). Following the operation the patient had a very satisfactory convalescence; on the eleventh postoperative day the choked disks were markedly diminished and her general condition was excellent.

Histologic examination of the fresh tissue which was removed at operation revealed a typical cellular type of ependymoma. The cells were closely packed together and were remarkably uniform in appearance. The nuclei were larger than those of astrocytomas, and the distribution of the chromatin granules was different. The architecture of the tumor also was characteristic as the cells were distributed uniformly throughout the tumor except around the blood vessels, where there was an acellular homogeneous zone. When the polychrome methylene blue stain was used we were unable to see fibrils around the blood vessels. There were a few mitotic figures which suggested that the neoplasm was actively growing, but it is not on this account that we have used the term "cellular type of ependymoma." These observations were confirmed by examination of sections which were stained with hematoxylin and eosin, with Mallory's stain (phosphotungstic acid hematoxylin), with Cajal's gold chloride and sublimate method, and with Hortega's method (ammoniacal silver carbonate). In addition, we found some regions in which the cytoplasm of the cells seemed to be missing; in these regions the tumor had a honeycomb appearance which usually is associated with oligodendrogliomas. We have noted this tendency in a previous study but only occasionally have we been able to prove that the cells are really oligodendroglial cells. We have preserved the original sections which were stained with polychrome methylene blue by the method we have described elsewhere, namely the simple expedient of sealing the coverglass with a solution of "duco." In the sections of the fresh tissue there were no regions in which the cells had a honeycomb appearance, yet the fresh sections had been cut from the same block of tissue which was fixed in solution of formaldehyde embedded in paraffin and used for the sections which were stained with hematoxylin and eosin. It would thus seem that the honeycomb appearance is the result of fixation and not the normal status of the cells.

Ependymomas of the fourth ventricle grow slowly and sometimes produce localizing signs before they produce any evidence of intracranial hypertension. In the following case, throbbing pain and dizziness which occurred on turning brought the patient to his physician, who suspected a tumor of the brain:

CASE 4.—A man aged 40 came to the clinic because of severe throbbing in the back of his head. Ten months previously, while playing golf, he became dizzy when he stooped over and shortly after this he had begun to vomit after almost every meal. Six months before he came to the clinic he had begun to have a severe thumping pain at the base of the skull; he had felt dizzy on arising and sudden attacks of dizziness and vomiting had occurred when he turned suddenly. The roentgenograms of the head were negative; examination of the eyes revealed that vision, the visual fields and the ocular fundi were normal. Neurologic examination revealed mild nystagmus and slight incoordination on the left side. Ventriculograms revealed internal hydrocephalus. A suboccipital craniotomy disclosed a large granular tumor which projected below the vermis and to the level of the first cervical vertebra. Biopsy, which was performed during the operation, disclosed that the tumor was an ependymoma. It was possible to elevate the

lower portion of the tumor and the entire tumor was removed in small pieces. Three years after the operation the patient was well and working every day.

Histologic examination revealed that the greatest portion of the tumor was of the cellular subtype but that here and there throughout the neoplasm were cavities or spaces that were lined with ependyma. The cells lining these spaces had a low columnar, epithelial appearance. The tumor was essentially a slowly growing one, as there was no evidence of mitotic figures or hyperchromatic nuclei and the cells and the nuclei were remarkably regular in size. In a few places the cytoplasm of the cells seemed to be missing and the tissue had a honeycomb appearance commonly seen in oligodendrogliomas.

The malignancy of a medulloblastoma is not the same in all cases; in some adults the malignancy is low. These tumors also are radiosensitive; therefore, partial removal and irradiation frequently are followed by prolonged relief.

**CASE 5.**—A woman aged 27 came to the clinic complaining of pain in the head in the occipital region and loss of vision. Eight months before she came to the clinic she had noticed pain in her head on bending forward. The pain had become worse and for four months before she came to the clinic she had been having projectile vomiting with the headaches. One month previous to her examination at the clinic she had begun to have intermittent diplopia and blurring of vision, associated with a roaring sensation in the left ear. Acute bilateral choked disks of from 3 to 4 diopters were found and neurologic examination revealed a moderate ataxic gait and slight incoordination. Suboccipital craniotomy was performed; the cerebellar convolutions were normal but the inferior tonsils were herniated through the foramen magnum. Incision of the vermis disclosed a large tumor that filled the fourth ventricle (fig. 8). Microscopic examination of a specimen of the tumor, which was made during the operation, revealed that the lesion was a medulloblastoma. It contained spongioblasts and had the appearance of a very malignant tumor with mitotic figures. Subtotal removal of the tumor was accomplished with the electrosurgical unit, sucker and curet. Air then could be seen bubbling through the aqueduct of Sylvius and into the fourth ventricle. Following the operation the patient was given three courses of high voltage roentgen therapy. She remained perfectly well for one year after the operation. She lived six years after the operation. One course of roentgen therapy was given each year. The patient was perfectly well; she was able to do her own housework and to work in her garden. She died suddenly a few days after the symptoms recurred.

#### IRRADIATION

There is probably no other group of tumors in which postoperative irradiation is as important as it is in the tumors of the cerebellum and fourth ventricle. At times we are dealing with a tumor which is highly radiosensitive, that is, a medulloblastoma, and in which it has been suggested that no operation should be done but that the patient should be subjected to at least three courses of irradiation. In some of the foreign clinics, wherever increased intracranial pressure without localizing signs develops in a child, irradiation is advised without operating. We do not agree with this procedure because in some cases of the more radioresistant types of tumor in which the history reveals that the tumor has been present only a short time it can be removed and a cure accomplished. However, in view of the fact that the majority of tumors which occur in the posterior fossa during childhood are medulloblastomas, irradiation after operation is usually indicated.

Cutler, Sosman and Vaughan<sup>11</sup> reported twenty cases of cerebellar medulloblastoma and reviewed sixty-one cases reported by Cushing in 1929. In all

except one case the diagnosis was confirmed by biopsy or by microscopic examination at necropsy. Medulloblastomas implant themselves in the pathway of the cerebrospinal circulation. These authors recommended irradiation of the entire cerebrospinal axis and the use of high voltage roentgen therapy and the administration of a maximal dose to each portal. Because of the sensitivity of the tumors to roentgen therapy the authors said that roentgen irradiation can be used as a therapeutic method for the differential diagnosis of cerebellar lesions which affect children. They recommended a trial of roentgen therapy before cerebellar exploration is undertaken.

Elsberg and Gotten<sup>12</sup> reviewed a series of twenty-three histologically verified medulloblastomas to determine whether conservative surgical procedures, which were characterized by wide decompression and followed by roentgen therapy, or more radical operation or surgical eradication of the tumor plus roentgen therapy gives the best results from the standpoint of operative mortality and survival. They found that the average period of survival of all patients who recover from one or



Fig. 8.—An unusually well encapsulated medulloblastoma of a low grade of malignancy.

more operations was seventeen and three-tenths months. In the ten cases in which only a conservative operation was done the average period of survival was seventeen and a half months, which is a factor of importance in favor of conservative operation for cerebellar medulloblastomas. They expressed the opinion that the immediate effect of the radical operation is apparently produced by the decompression rather than by the complete removal of the tumor and that the length of survival is a consequence of the roentgen therapy of these radiosensitive growths. They concluded that in the treatment of cerebellar medulloblastoma conservative operation has produced better immediate results than has an attempt at radical extirpation and that from the standpoint of length of survival the former procedure has produced results which are at least as good as those obtained with the radical method.

Elsberg, Davidoff, and Dyke<sup>13</sup> have advised roentgen irradiation of tumors in the operating room while the wound is open. They said that medulloblastomas, which occur frequently in the posterior cranial fossa of children, have a vascular base which practically can

12. Elsberg, C. A., and Gotten, Nicholas: The Results of Conservative Compared with Radical Operations in the Cerebellar Medulloblastomas: An Analysis of Twenty-Five Cases, *Bull. Neurol. Inst. New York* 3: 33-52 (June) 1933.

13. Elsberg, C. A.; Davidoff, L. M., and Dyke, C. G.: The Roentgen Treatment of Tumors of the Brain in the Operating Room by Direct Radiation Through the Open Wound, *Bull. Neurol. Inst. New York* 6: 19-32 (Jan.) 1937.

11. Cutler, E. C.; Sosman, M. C., and Vaughan, W. W.: The Place of Radiation in the Treatment of Cerebellar Medulloblastoma: Report of Twenty Cases, *Am. J. Roentgenol.* 35: 429-453 (April) 1936.

never be removed completely and said that a survival period of more than two years is exceptional. Medulloblastomas are very radiosensitive and the results of some occipital decompression for relief of obstructive hydrocephalus, followed by roentgen therapy without any attempt at radical removal of the growth, are as good as if not better than the removal of a large amount of tumor. In all cases of cerebellar tumors they advocated the direct roentgen therapy while the wound was open.

Sachs, Rubinstein and Arneson<sup>14</sup> expressed the opinion that medulloblastomas are definitely influenced by roentgen therapy. In a series of thirty-five cases of medulloblastoma, fifty-two operations were performed. The mortality on the basis of the number of cases was 28.5 per cent. Of the patients who were operated on but who did not receive roentgen therapy, one lived seven months and all the rest died within a shorter time. In the group of cases in which radical operation and roentgen therapy were used, one patient lived fifty-four months, one is still living at the end of seventeen months and one is still living at the end of fourteen months. The operative notes reveal that in this group of cases a thorough extirpation had been done. Necropsy on the patient who lived twenty-nine months disclosed a small local recurrence in the cerebellum. This had not caused any symptoms. Necropsy also disclosed an extensive tumor meningitis which extended the entire length of the spinal cord. They drew the conclusions that roentgen therapy should be preceded by radical operative removal and that high voltage roentgen therapy prolonged the life of patients who have a medulloblastoma.

#### SUMMARY

Tumors of the fourth ventricle do not produce a typical clinical syndrome. However, increased intracranial pressure, a high degree of choked disk, vomiting without nausea, and intermittent severe headache should always suggest a tumor of the fourth ventricle. The treatment consists of suboccipital craniotomy with removal of as much of the tumor as is compatible with the condition of the patient. Postoperative roentgen therapy should depend on the type of tumor found and the amount removed at operation. The use of frozen sections and staining with polychrome methylene blue have made possible the differential diagnosis of tumors of the fourth ventricle at the operating table. This aids in determining the proper surgical procedure.

#### ABSTRACT OF DISCUSSION

DR. F. R. TEACHENOR, Kansas City, Mo.: From these statistics one is impressed with the fact that the tumors encountered are not an exceedingly encouraging group. The statistics are not exactly comparable on account of the different varieties of their statistical tables, with the exception of the astrocytomas, which one naturally expects to give a better prognosis. The prognosis in the medulloblastomas of the fourth ventricle is not a good one. I will confine my remarks to the practical side of the treatment of tumors of the fourth ventricle as far as irradiation and surgery are concerned. Davidoff and Dyke, Cutler and Sosman, and others are recommending the use of irradiation entirely in the treatment of the medulloblastoma. It seems obvious from the symptoms as outlined by Drs. Craig and Kernohan that there are positive means of preoperative diagnosis of the medulloblastoma over any of the other varieties of posterior fossa tumors. In addition to that, one must consider the cases in the stage in which one receives them. Certainly if the

patient is received in the early stage before pressure signs are present one is entirely justified in utilizing irradiation preoperatively. If the patient improves under irradiation, I think it quite consistent that operation be postponed or probably not performed. Most of the patients that I see come in a late stage of compression and approaching a terminal condition. In these instances I do not believe that one is justified in utilizing the x-rays alone but feel that operation is the method of choice and, if the medulloblastoma is the tumor found by microscopic examination, postoperative irradiation of the entire cerebrospinal axis is the best method of treatment. I agree that with the medulloblastoma in childhood below the age of 15 the prognosis as to life is much shorter than above 15. In my experience, two years or two and one-half years is about the limit in children under 15, while of those above I have one that lived five and one-half years with rather interesting symptoms. The patient was first operated on at another clinic for a cerebellar tumor the character of which I did not know, but I saw her some three and one-half years afterward with signs of a tumor of the spinal cord, the symptoms of which came up rather suddenly. I suspected a medulloblastoma, but on account of the suddenness of the onset of the symptoms I removed a pedunculated tumor from the tip of the conus and extended the active life of the patient for a year and a half. I believe that in most instances, particularly in the later stages of the disease, the operative procedure followed by irradiation is the choice, and even though it does cause additional seeding, if the tumor is removed in sufficient quantities to break the block and reestablish the circulation of the cerebrospinal fluid certainly the life period is extended thereby, and with irradiation it may be prolonged.

DR. F. C. GRANT, Philadelphia: In their discussion of the midline cerebellar tumors, the authors did not stress a clinical symptom which is important. Children with cerebellar tumors almost invariably have enlargement of the head. As the tumor interferes with the cerebrospinal fluid circulation, the lateral and third ventricles increase in size and intracranial pressure is raised. In children with incompletely ossified suture lines the sutures separate and the head enlarges. This separation of the sutures often accounts for the absence of choked disk and delays diagnosis. The symptoms of midline cerebellar tumor are notoriously fugitive and difficult to confirm. Absence of choked disk is enough to convince most pediatricians or neurologists that an intracranial lesion is not the cause for the clinical symptoms. But given a child who has bouts of morning headache and vomiting, is clumsy and falls off his roller skates or bicycle with increasing frequency, and in whom on examination nystagmus is absent and signs of incoordination vague and generalized, one should always examine the head. If it seems large and if a cracked-pot sound can be demonstrated, separation of the sutures has occurred and the suspicion that an intracranial lesion exists should be definitely entertained.

DR. W. McK. CRAIG, Rochester, Minn.: One of the penalties of trying to crowd into fifteen minutes a review like this is that some of the important points are omitted, and it is gratifying to have the presentation rounded out by such generous discussion. In treating any type of tumor of the brain the sociologic aspects must be considered. In contemplating surgical measures, one should not forget that they depend on the condition of the patient and on the stage of development of the symptoms. We would like to operate on these patients in the early stages of development of the tumor and remove all of it, but many factors decide whether the operative procedure should be radical, modified or conservative, and sometimes palliative irradiation is indicated, depending, as Dr. Teachenor mentioned, on the stage of development of the tumor at which the patient is brought in for treatment. The value of decision at the operating table, I think, has been greatly enhanced by biopsy and diagnosis of fresh tissue. Knowledge of the type of tumor helps decide between radical and conservative operations. Surgical limitations were illustrated by the fact that, of the eighty-two cases, in only twenty were the tumors totally removed. Of the cases of medulloblastoma, there were thirty in which subtotal removal, and one in which total removal, were influenced by diagnosis of fresh tissue. In the twenty-one cases of ependymoma, there were thirteen subtotal removals and eight total removals, the condition of the patient limiting the opera-

14. Sachs, Ernest; Rubinstein, J. E., and Arneson, A. N.: Results of Roentgen Treatment of a Series of One Hundred and Nineteen Gliomas, Arch. Neurol. & Psychiat. 35: 597-615 (March) 1936.

tion. In the nineteen cases of astrocytoma, there were fifteen in which removal was subtotal and four in which it was total, and in all three cases of hemangio-endothelioma removal was total. Whenever any uncertainty existed as to whether tumor tissue was left behind, removal was indexed as subtotal. I should like to leave the impression that the operative procedure and the results of the operation depend a great deal on the condition of the patient. Our best results were realized in those cases in which diagnosis was made early, a radical procedure was carried out and there had been no irreparable damage to the brain. Dr. Grant's point is very important. We neglected to comment on the appearance of the patient, especially the size and position of the head. One must consider the appearance and the general condition of the patient in determining the surgical approach to the problem.

## AN ACUTE INFECTION OF THE RESPIRATORY TRACT WITH ATYPICAL PNEUMONIA

A DISEASE ENTITY PROBABLY CAUSED BY  
A FILTRABLE VIRUS

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Infections of the respiratory tract are among the most common afflictions of mankind, and pneumonia, which occasionally accompanies or follows them, is the third most common cause of death in the United States. Any progress made in the knowledge of such infections is therefore urgently needed.

Only recently has the physician been armed with comparatively simple methods for the diagnosis of one of these diseases, epidemic influenza, which is now known to be caused by a filtrable virus. Methods for isolating and identifying the virus of the common cold are still too complicated for the average clinical laboratory in routine diagnosis. The discovery of the causative agent of influenza permits separation of the disease as an entity from the undifferentiated group of infections of the respiratory tract and provides a standard, so to speak, against which other entities may be compared. The discovery also confirmed a long established impression gained on clinical and epidemiologic grounds that influenza is a disease entity caused by a filtrable virus.

From studies already made on the group of acute infections of the respiratory tract other than influenza, it is predictable that it is composed of a number of specific entities probably caused by filtrable viruses which remain to be identified, perhaps by methods similar to those by which the viruses of influenza and the common cold were discovered. Efforts in this direction no doubt will eventually make possible a classification of this important group of infections such as has been made with fruitful results in the case of pneumonias of bacterial origin.

With these points in mind, I studied a group of seven cases of an unusual form of tracheobronchopneumonia and severe constitutional symptoms which occurred in 1938. The clinical symptoms and signs of the infection were so uniform in these cases and yet so different from those of other common diseases that I was led to regard the disease as an etiologic entity caused by an unknown agent. I have learned from my colleagues that similar cases were encountered by them in New York, Boston, Philadelphia and elsewhere in 1938. The condition was usually called influenza.

From the Jefferson Medical College and Hospital.

### REPORT OF CASES

CASE 1.—H. M., a man aged 44, did not feel well March 3 while in New York. The next day he felt chilly and hot alternately and noticed a slightly sore throat. He went to bed for two days and was thought by his physician to have influenza. There was profuse sweating. He returned to work but on March 7 had a recurrence of chilly sensations and perspiration. Cough with a slight amount of yellowish sputum developed. He then came to Philadelphia, and entered the hospital on March 8, about the fifth day of illness, as a patient of Dr. Guy Nelson.

He was a robust, severely ill man. His face was flushed and his pharynx inflamed. There were occasional periods of coughing, but no sputum was raised. The heart and abdomen were normal. A few rales were present in the interscapular regions. The temperature, pulse rate and respiratory rate are shown in figure 1. The leukocytes numbered 8,000. A diagnosis of tracheobronchitis was made.

During the first week of observation the temperature remained continuously high, but in contrast the pulse rate was low. There were a frequent hacking cough with scanty mucopurulent sputum, sweating, slight hoarseness, restlessness, abdominal distention, constipation and drowsiness. The patient complained of headache, photophobia and general aching. The breath sounds were suppressed in the base of the left lung posteriorly, where a few rales were heard. The number of leukocytes rose to 11,800. Typhoid was strongly suspected, but no agglutinins for *Bacillus typhosus* were ever demonstrable, and the bacilli were not found after repeated blood cultures and stool examinations.

About the twelfth day of illness the patient was drowsy, perspired freely and coughed occasionally, and the hoarseness had progressed to aphonia. The abdomen was distended, and

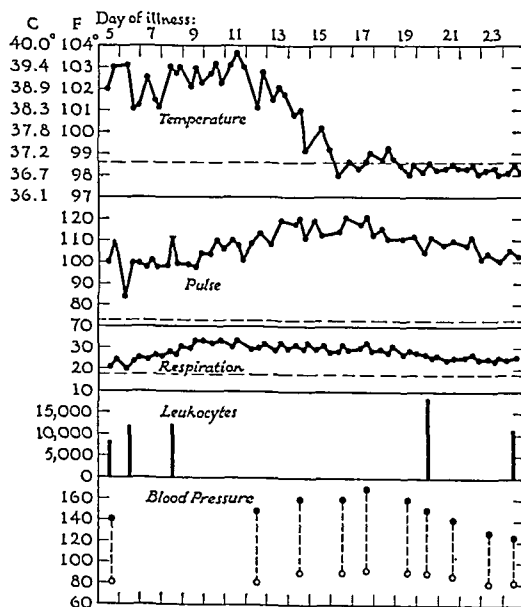


Fig. 1 (case 1).—Clinical course. The pulse rate, respiratory rate and leukocyte count were comparatively low in the first week.

the pulse and respiratory rates were increased (fig. 1). The conjunctivas were injected, the tongue was heavily coated and anorexia was present. Two diarrheal bowel movements occurred. The patient was apprehensive at times, drowsy at others and disoriented, especially at night. With the abdominal distention there was a brief attack of acute pain in the left upper quadrant. The patient was extremely ill, and typhoid was still suspected although no proof was forthcoming. A roentgenogram of the lungs showed a faint increased mottling, especially in the right lung.

For the next few days the temperature declined and the pulse rate rose. Profuse sweating continued. Tachypnea continued, and slight dyspnea and cyanosis developed. Aphonia persisted, and the nasal passages became obstructed by acutely inflamed and swollen mucous membranes. The pharynx was dry and



inflamed. Many rales in the base of the left lung and a few in that of the right were now heard. The breath sounds were harsh, but no other abnormal signs except pleural friction were audible in the left axilla. Another roentgenogram, made on the sixteenth day after the temperature reached normal, showed an increased mottled density in both lungs, but particularly on the right side, suggestive of diffuse pneumonia. Garglings

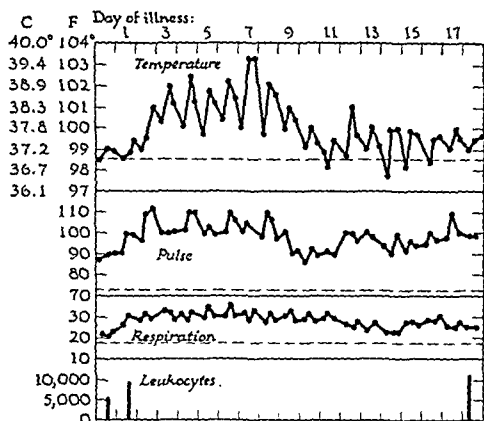


Fig. 2 (case 2).—Clinical course from the first day of illness.

of material from the nasopharynx were made at this time and dropped into the nares of ferrets by Drs. Stokes and Francis, but no virus was isolated.

Numerous rales in the base of the left lung and fewer in that of the right persisted with diminishing intensity. Tachycardia and tachypnea persisted for three weeks after the temperature became normal. The patient lost 12 Kg. (27 pounds) in weight.

Two weeks later, because of persistent aphonia, laryngoscopic examination was performed by Dr. Calvin Fox. The epiglottis, arytenoid processes, vestibule of the pharynx and tracheal wall were inflamed. The vocal cords were congested and thick. Roentgenograms made on the twenty-seventh and seventy-second days showed that the mottling had disappeared, but a haziness over the base of the left lung suggested pleural thickening.

**Laboratory Data.**—The leukocyte counts are shown in figure 1. The percentage of polymorphonuclears was found to be increased to 80 or 90 at each examination. Three blood cultures were negative, and agglutinins for *Bacillus typhosus*, *Brucella melitensis* and *Pasteurella tularensis* were absent. Numerous examinations of sputum and material obtained by swabbing the throat showed the usual nasopharyngeal flora, with *Streptococcus hemolyticus*, *Streptococcus viridans*, *Streptococcus hemolyticus*, diphtheroids, staphylococci, gram-negative cocci and bacilli and on one occasion pneumococcus type XIX. No tubercle bacilli were found. Febrile albuminuria was present. Blood serum



Fig. 3 (case 2).—Appearance on the seventh day of illness. There is a diffuse mottling throughout both lungs, more marked on the right. The interlobar pleura on the right is thickened.

obtained on the sixteenth, thirty-third and seventieth days after the onset of illness and tested by Dr. Francis did not contain antibodies for epidemic influenza virus.

**Summary.**—This patient became ill with the symptoms of a sore throat, recovered to some extent but became worse again and exemplified the so-called typhoid state with tracheitis and bronchitis. Although rales were present in the lungs early in the course of the disease, symptoms and signs of massive inva-

sion were delayed until after the temperature had declined, about the twelfth day. The signs persisted long after the fever disappeared. These observations and persistent laryngitis, hoarseness, aphonia, sweating, dyspnea, cyanosis and drowsiness were the main features. The illness lasted sixteen days.

**CASE 2.**—M. S., a man aged 39, had a herniorrhaphy performed February 25. Convalescence was uneventful until March 11, when he thought he was getting a cold. There was stuffiness of the nose, and pain developed in the left side of the chest. No abnormal signs were present in the lungs. The patient was allowed out of bed, but his discomfort persisted. March 13 he felt generally uneasy, ached all over and felt "grippy." A drenching sweat occurred that night and another on the following night. Fever was noted first March 14 and increased to 38.3 C. (101 F.) the next day, as shown in figure 2. On the third day of fever, sharp pain developed in the lower anterior part of the right axillary region, which was worse on breathing. It became so severe that opiates were required to control it. A few rales were present in this area. The respiratory rate increased to 32. The pharynx was inflamed but was not painful. The leukocytes numbered 9,000.

During the next few days the number of rales increased and the breath sounds were suppressed in the base of the right lung. Occasional pain occurred in the root of the neck on the right side suggestive of the referred pain of diaphragmatic pleurisy. There was no cough and no sputum. Rales appeared in the base of the left lung. Epistaxis occurred on the sixth day.

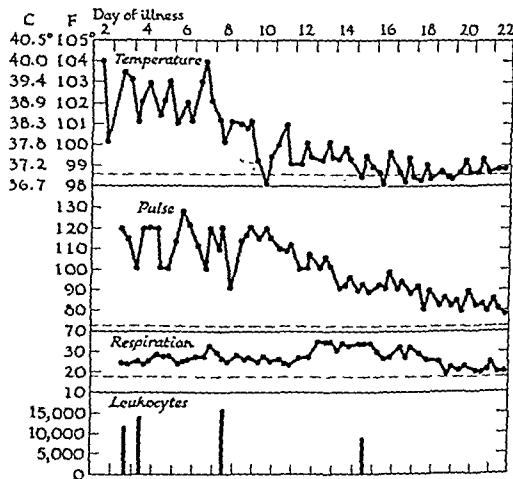


Fig. 4 (case 3).—Clinical course.

The abdomen was distended and constipation was present. A roentgenogram of the chest (fig. 3) made on the eighth day showed diffuse increased mottled shadows throughout both lungs, more prominent on the right side, suggestive of diffuse pneumonia (Dr. Karl Kornblum). The interlobar pleura was thickened on the right side, and density at the base suggested a small collection of fluid. At about this time the patient complained of pain and numbness in the right wrist, elbow and shoulder. His legs and teeth ached. There was profuse sweating most of the time. One night his gown was changed fourteen times. Physical signs of fluid appeared in the base of the right lung. Dyspnea and cyanosis appeared and became distressing, but there was no cough or sputum. Nasopharyngeal secretions were obtained about this time by Drs. Kinney and Magill and inoculated intranasally into ferrets, but no virus was recovered. A blood culture was sterile. The temperature began to decline after the eighth day, and the patient improved. Dyspnea, cyanosis and sweating diminished. Atropine sulfate controlled the excessive perspiration. A symmetrical patch of hyperesthesia 3 or 4 inches in diameter was noted on the anterior surface of both thighs. The patient began to cough occasionally on the eleventh day and felt that his nose was plugged up again.

A small fleck of blood-tinged tenacious sputum was raised, which contained *Streptococcus viridans*, *Streptococcus hemolyticus*, *pneumococcus* type XIX, diphtheroids and gram-negative cocci.

Thoracentesis was performed, and 300 cc. of bloody, turbid fluid, which was sterile on culture, was obtained. The process was repeated three days later and again on the twenty-second day. Fluid of similar quality and quantity was removed. On the nineteenth day a roentgenogram showed a diminution of the density of the infiltration seen previously. There was an irregular density at the base of the right lung, and there were a few patches of density in the base of the left lung. Low grade fever persisted. Several weeks later a trocar and drain were inserted by Dr. Nassau. The fever increased, and on the fifty-third day the patient suddenly died. Necropsy was not performed.

This patient was observed from the first day of illness; this began as an ordinary infection of the respiratory tract, but profuse perspiration and severe pleuritic pain developed. Evidence of pulmonary invasion appeared about the fourth day and rapidly involved both lungs. Sterile pleural effusion was present. The chief features were the diffuse atypical pneumonia, drenching sweats, dyspnea, cyanosis, severe pleuritic pain and a minimal amount of cough and sputum.

Nasopharyngeal washings were obtained on the eighth day of illness, too late, perhaps, according to the experiences of British investigators,<sup>1</sup> for a virus to be obtained. The blood serum did not contain antibodies for the virus of epidemic influenza.

Experience with these two patients led me to suspect that I was dealing with an unusual form of infection, so that when the next patients were seen, while the first two were still under observation, attempts were made to obtain a virus earlier in the disease. March 20 and March 22, nasopharyngeal washings were obtained at my request from patients 1, 2, 3 and 7 by Drs. Stokes and Kinney of the University of Pennsylvania and Dr. Francis and Magill of the Rockefeller Institute.<sup>2</sup>

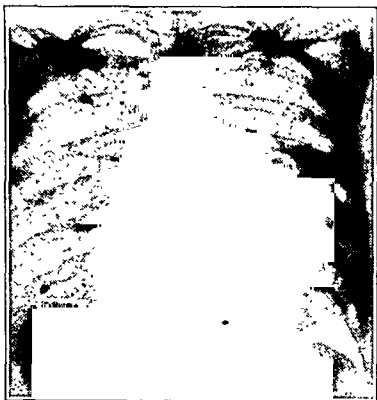


Fig. 5 (case 3).—Appearance on the fifth day of illness. The hilar shadows are increased in density. There is a diffuse mottling in both lungs, with a denser shadow in the middle of the left lung field.

CASE 3.—Mrs. K. A., aged 48, first noticed a "head cold" March 12. Her brother had a similar infection at the same time. The patient, her brother (patient 4), her son (patient 5), a friend (patient 6) and her mother (patient 7), among others, were together at a party March 12. Mrs. K. A. felt unduly warm at the time and had chilly sensations the next day, but disregarded them. During the following days the symptoms of a cold persisted, and March 17 they became worse. March 18, fever and coughing began. Chilly sensations recurred, and pain developed in the left side of the chest. The temperature rose to 40 C. (104 F.). The patient was admitted to the hospital on the third day of severe symptoms (fig. 4).

At examination she was restless, apprehensive and overalert. There were slight cyanosis and a hacking, nonproductive cough. The pharynx was slightly inflamed. Marked hyperesthesia was present over both mammary regions. Rales were heard in both interscapular areas and in the bases of both lungs. There was tenderness in the right upper quadrant of the abdomen. The leukocytes numbered 11,800; 81 per cent were polymorphonuclear cells. A blood culture was sterile. Cultures of naso-

pharyngeal secretions obtained with a throat swab showed *Staphylococcus albus* and pneumococcus type IV among other forms of bacteria. A roentgenogram revealed an increase in the usual density of the hilus and vascular markings in both lungs. The temperature and pulse rate were high (fig. 4).

The next day more rales were heard in the base of the right lung and the breath sounds had a faintly tubular sound. Nasal washings were made by Dr. Kinney on the fourth day of illness and inoculated intranasally into ferrets. A virus was isolated.

On the fifth day the patient was severely ill and was stuporous at times. Many rales, egophony, pectoriloquy, weak bronchophony and tubular breathing were now heard in the base of the left lung. There was slight rhythmic flaring of the alae nasi. X-ray examination revealed a diffuse density in the mid-portion of the left lung

(fig. 5) and an increase in the hilar shadows noted two days before which was suggestive of diffuse bilateral pneumonia. During the next few days the patient became considerably worse. On the sixth day, after being urged to raise sputum, she raised the first sample of bloody, tenacious sputum, which contained *Streptococcus viridans*, *Streptococcus hemolyticus*, gram-negative cocci and a few type IV pneumococci. Throat washings were obtained at this time by Dr. Magill and inoculated into ferrets. A virus was obtained which was apparently similar to the one obtained by Drs. Stokes and Kinney two days before.

The patient became irrational. Her face was flushed, the mucous membranes were cyanotic and the lining of the mouth, which had felt uncomfortable for several days, was spotted with bright red discrete and confluent macules, some of which contained papules and whitish speckles. Coarse rales were heard in both mammary regions. Pleuritic pain and friction sounds were present in the left axilla. Dyspnea was severe and she appeared to be gravely ill. Oxygen therapy relieved the dyspnea and cyanosis considerably. On the eighth day euphoria and overalertness, with slight mental confusion and disorientation, developed. The skin over the mammary region was hyperesthetic; touch-

ing and pinching it caused pain. There was tympany in the left mammary region but no rales were heard. Posteriorly there was dullness in the base of the left lung, with decreased tactile fremitus, loud bronchial breathing, egophony and pectoriloquy. A small area where weak bronchial breathing and rales were heard was found in the right base. The leukocytes numbered 15,800.

On the ninth day muscae volitantes and headache were complained of and the patient became more drowsy. She slept most of the time and appeared to be toxic. Various groups of muscles twitched from time to time. The reflexes were generally hyperactive, especially the patellar reflexes. Encephalitis was suspected, but the spinal fluid was normal in all respects and contained two leukocytes per cubic millimeter.

Gradual improvement then began. Herpes appeared on the lip. A roentgenogram on the thirteenth day showed that

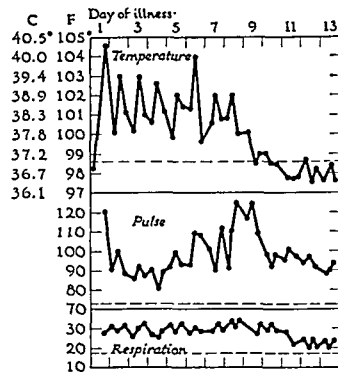


Fig. 6 (case 7).—Clinical course from the first day of illness. Note the low pulse rate.

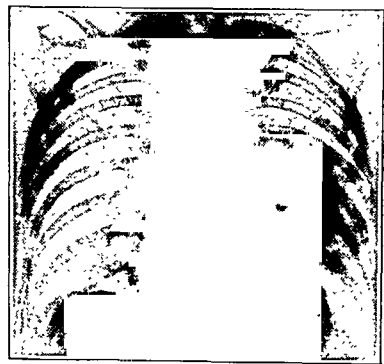


Fig. 7 (case 9).—Appearance on the fourth day. There is a large area of density in the left lung. The left dome of the diaphragm is slightly elevated. The root shadows on the right side are denser than normal.

1. Stuart-Harris, C. H.; Andrewes, C. H., and Smith, W., with Chalmers, D. K. M.; Cowen, E. G. H., and Hughes, D. L.: A Study of Epidemic Influenza with Special Reference to the 1936-1937 Epidemic, Medical Research Council, Special Report Series, No. 228, London, His Majesty's Stationery Office, 1938.

2. Drs. Stokes, Kinney, Francis and Magill performed most of the animal and serologic tests.

the lungs had become relatively clear except for haziness at the base of the left one suggestive of pleural thickening. The number of leukocytes dropped to 9,000.

Improvement was rapid after the sixteenth day, and the patient left the hospital on the twenty-fifth day for further convalescence. She had lost about 7 Kg. (15 pounds) in weight. Rales and friction sounds were still present in the

base of the left lung. She was reexamined on the forty-third day. Her temperature was 37.3 C. (99.2 F.) and she felt weak. A roentgenogram showed thickening of the interlobar pleura between the upper and lower lobes of the left lung but no other abnormalities.

**Summary.**—The illness apparently began as a mild infection of the upper part of the respiratory tract, which was followed after several days by severe tracheobronchitis and diffuse pneumonia. In spite of the

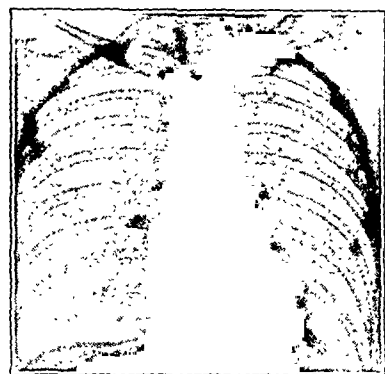


Fig. 8 (case 9).—Appearance on the tenth day. The patch of density in the left lung shown in figure 8 has disappeared, but there is now a diffuse mottling of both lung fields. Plates made on the twenty-third and forty-third days showed progressive diminution of the abnormal densities until the seventieth day, when the lung fields appeared normal.

pulmonary involvement and hacking cough there was practically no sputum. Dyspnea, cyanosis, photophobia, stupor, nervous symptoms and pleuritic pain were conspicuous characteristics. Sweating was not prominent. Rales and roentgenographic evidence of pleural involvement were still present two weeks after the temperature became normal. The type IV pneumococci recovered from the sputum were regarded as commensals without significance.

Nasopharyngeal washings from which an apparent virus was recovered were obtained on the fourth day by Dr. Stokes and on the sixth day by Dr. Francis. Blood serum for tests was

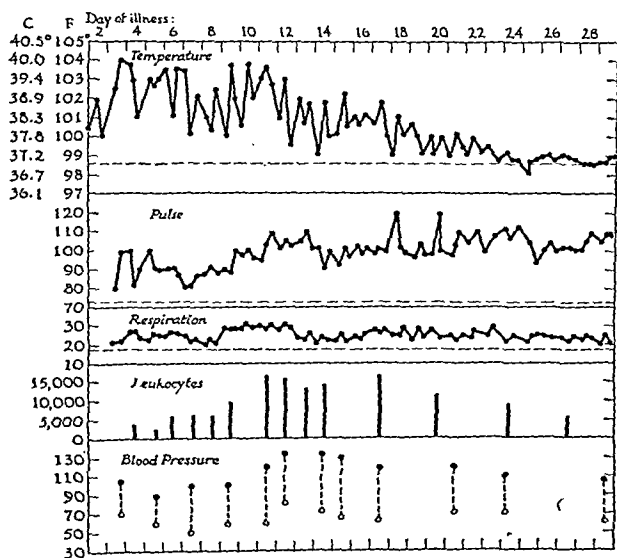


Fig. 9 (case 9).—Clinical course from the second day of illness. Note the low pulse rate and the low leukocyte counts early in the illness. The blood pressure rose during the course.

obtained on the same days, on the forty-third and on the one hundred and twentieth day but contained no antibodies for the virus of epidemic influenza.

Patients 4, 5, 6 and 7, as mentioned, had been in contact with patient 3 when they attended a gathering March 12 at which several members of her family and

a few friends were present. Mrs. A. (patient 3) and her brother did not feel well at the time. Within the next week Mrs. A.'s son, a friend and her mother became ill.

**CASE 4.**—Mr. B. (brother), aged 45, became ill about March 12, feeling cold, shivery and "grippy." He kept on working except for one day in spite of his illness, which lasted about two weeks. There was an annoying dry cough but no sputum. He was examined twice about the ninth day of illness by Dr. Burgess Gordon, who noted rales in both interscapular regions on both occasions. The temperature, taken on two occasions, was normal.

**CASE 5.**—J. A. (son), aged 25, noted dryness of the throat March 14. Two days later the throat was very sore. Rhinitis, malaise and muscle pains were present. It hurt to bend the neck forward. The patient did not go to bed. There was no fever or cough. These symptoms lasted three days and gradually disappeared, so that by the eighth day only soreness of the muscles of the neck was noted.

**CASE 6.**—Dr. C., aged 57, a friend, had rhinitis and sneezing March 16. He felt hot but did not take his temperature. He continued to work but the next day did not feel well. There were epigastric pain, cough with a small amount of sputum, slight diarrhea and pain. When the temperature rose to 38.3 C. (101 F.) he went to bed. There were headache, anorexia, a disinclination to move and muscle pains "as in influenza." The patient recovered after four days.

The symptoms of patients 4, 5 and 6 would generally be regarded as those of a cold and agree with the criteria laid down by Stuart-Harris and his associates<sup>1</sup> for what

they call the febrile catarrhs as differentiated from influenza. It would be highly valuable to know whether a single virus caused this "house" epidemic of disease of the respiratory tract, in which patients 3 and 7 had a severe form, and the others had a mild form. The fact that mice inoculated with nasopharyngeal washings from patient 3 and with blood serum from patient 7 seemed to be made ill by a similar filtrable infectious agent lends support to the hypothesis.

Attempts to solve the problem by immunologic methods are under way.

**CASE 7.**—Mrs. B. (mother), aged 76, noted dryness of the throat and cough about March 16. I saw her March 19, at which time her face was flushed and she appeared to be ill although her temperature was 36.1 C. (97 F.). In the afternoon she became much worse. There was no chill, but the temperature rose to 40.3 C. (104.5 F.) and she was put to bed. She was somnolent and confused, failed to cooperate and was incontinent of feces and urine. She remained at home and was attended by Dr. Burgess Gordon. He found evidence of extensive bronchitis and rales in the base of both lungs. During the next few days high fever persisted, the pulse rate was low and the respiratory rate was 30 per minute, as shown in figure 6. The patient perspired profusely, was cyanotic and coughed but raised no sputum. Pharyngeal exudate was obtained by a swab and inoculated into a mouse. Type IV pneumococci were present. There was constipation, and about the sixth day tympanites, present from the beginning, became severe, tachycardia developed, and the patient appeared to be



Fig. 10 (case 11).—Appearance on the twenty-first day of illness. There are disseminated nodular areas of density in both lung fields. The shadows in the bases, especially in the right, suggest consolidation.

moribund. She was comatose up to the eighth day and confused mentally for a week thereafter. After the eighth day the temperature declined and recovery ensued.

Nasopharyngeal washings were obtained on the fourth and sixth days by Drs. Kinney and Stokes and Magill and Francis, but no virus was obtained. However, blood serum inoculated intracerebrally into white mice by Dr. Francis caused the mice to become ill after twelve or eighteen days. An occasional animal died. The virus apparently died out after the fourth passage.

Patients 8, 9, 10 and 11 were seen in May, June and August and had had no contact with the patients previously described or with any one else with a similar disease. Patient 8 was regarded as having influenza, and in case 9 suspicion of typhoid or psittacosis led to a delay in obtaining nasopharyngeal washings to be examined for a virus until the eighth day.

CASE 8.—Dr. H. C., aged 27, a patient of Dr. George Major of Reading, Pa., had a feeling of malaise, dryness of the throat which developed into a sore throat, hoarseness and cough in the afternoon of May 17. At 9 p. m. a chill occurred, and the temperature then rose to 40 C. (104 F.). The patient had to go to bed, but the next morning there was a remission of symptoms and he resumed his work. He felt fairly well until evening, when fever and malaise returned. For the next few days there were great prostration and weakness and the temperature hovered about 40 C. (104 F.), the pulse rate between 100 and 110, the respiratory rate between 20 and 40 and the leukocyte count between 7,000 and 12,000. The patient was extremely ill, perspired profusely and was greatly distressed by a continuous hacking, unproductive cough. There were photophobia, conjunctival injection and lacrimation. Small amounts of sputum were raised, and numerous cultures of it revealed staphylococci, Friedländer's bacilli and hemolytic streptococci but no type specific pneumococci. A blood culture was sterile.

I saw the patient on the seventeenth day of illness, at which time there was diffuse pneumonia and restlessness, apprehension, headache, sweating, nasal obstruction, cyanosis, severe dyspnea and cough, which were prominent features. Nasopharyngeal washings were made at this time and sent to Dr. Francis, who inoculated them into ferrets but failed to recover any virus. The blood serum contained no antibodies for the influenza virus.

During the second and third weeks of the illness the temperature declined, but the pulse rate rose to 120 and 130, the respiratory rate to 50 and the leukocyte count to 12,000 and 16,000. The temperature rose again to 38.9 C. (102 F.) on the twenty-second day and followed an irregular course, gradually becoming lower; it remained normal after the forty-first day.

CASE 9.—Miss H. A., aged 38, noted discomfort in the abdomen after a dietary indiscretion June 10. There was no diarrhea or constipation, and the discomfort disappeared after a few days. June 18 she had chilly sensations, and pain developed in both eyes. She was very sleepy June 19 and the ocular pain persisted. June 20 she was awakened by cough, chilliness, pain and soreness under the sternum. The temperature varied between 37.8 C. (100 F.) and 39.4 C. (103 F.). Chilliness recurred several times in the next day or two and was accompanied by sweating, which was perhaps caused partly by the taking of acetylsalicylic acid. Cough was frequent, but no sputum was raised. The patient was admitted to the hospital on the third day of illness.

The voice was slightly hoarse, and the mucous membranes of the eyes, nose and pharynx were reddened. The tongue was heavily coated. No abnormal sounds were heard in the lungs. There was slight abdominal distention. A tender lymph node the size of a hazelnut was palpable under the ramus of the mandible on the right side.

Because of the high fever, relatively slow pulse and leukopenia (4,800 cells), the patient was isolated as presumptively having typhoid.

The chief complaints in the first few days were pain in the eyeballs, photophobia, intense frontal headache and cough. There were hoarseness, congestion of the conjunctival and oral mucous membranes and duskiness of the face. Paroxysms of cough occurred frequently but were not productive. The patient was drowsy at times almost to the point of stupor, apart from the occasional narcosis from codeine given for headache.

No abnormal sounds were heard in the chest until the fourth day, when Dr. Tocantins detected harsh breathing and a few rales in the left infraclavicular region and a few rales in the left scapular region. A roentgenogram made at the bedside revealed a patch of increased density in the periphery of the left lung between the second and fourth ribs, and the left side of the diaphragm was somewhat high, as shown in figure 7. By request a small fleck of sputum was raised; it was raised with difficulty and contained a few indifferent streptococci, *Micrococcus catarrhalis* and diphtheroids.

When I examined the patient on the seventh day the only abnormal sign I could detect in the chest was diminished breathing in the left scapular area. The patient now had no complaints except headache, photophobia and cough, but she appeared to be gravely ill. On the eighth day a profuse drenching sweat occurred. Rales returned in the left lung, and the inspiratory breath sounds became harsh and sibilant. Sonorous and rasping sounds were heard. Dyspnea was present and cyanosis appeared. A roentgenogram showed that the localized density in the left lung had almost disappeared, but the whole left lung now seemed faintly clouded. The early density may have been caused by atelectasis. By this time it was obvious that the patient did not have typhoid, and the pharyngeal secretions were collected by Dr. Stokes and inoculated into ferrets. A small amount of white creamy sputum raised with difficulty was inoculated intraperitoneally into mice to determine whether the psittacosis virus was present and into guinea pigs to test it for tubercle bacilli. The leukocyte count remained low. On the seventh and eighth days the patient was given a total of 8 Gm. (120 grains) of sulfanilamide. There was no evidence of any effect.

During the next few days the cough was distressing and stupor was present but the patient was lucid on questioning. She lay on her right side to lessen the cough. Cyanosis deepened, and dyspnea was at times distressing. Vomiting occurred several times, there were periods of drenching perspiration, and headache and photophobia persisted. The spleen and liver were not felt. Abdominal distention and constipation were present.

Many rales, suppressed breath sounds and dulness were present in the lower part of the left lung and tympany above; suppressed breath sounds and wheezing were heard in the right side. A roentgenogram made on the tenth day showed a diffused mottling composed of nodular densities in both lung fields (fig. 8).

No unusual events occurred in the following few days except an occasional drenching sweat. Dyspnea and cyanosis persisted and were worse after coughing attacks. No sputum was raised. Oxygen greatly relieved the dyspnea. The temperature, pulse rate, respiratory rate, number of leukocytes and blood pressure during the illness are shown in figure 9. The pulse rate, low in the beginning, rose. The respiratory rate was never rapid. The blood pressure decreased temporarily and then increased. On the seventeenth day friction was palpable and audible in the lower anterior part of the right axillary area, where the patient complained of pain. Evidence of pleuritis disappeared after a few days. Flaring of the alae nasi was noted. In an attempt to get another sample of sputum Dr. Clerf made a laryngoscopic examination. The mucous membranes were found to be markedly congested and covered in places with a thick, white, tenacious exudate. Some of the exudate was obtained, cultured and inoculated into mice. The animals recovered. The leukocyte count rose to 17,000.

The patient improved gradually and the symptoms slowly disappeared, but tachycardia persisted and the tongue was heavily coated. A roentgenogram showed gradual clearing of the density in the lungs. Numerous rales and wheezes persisted. On the twenty-third day another profuse sweat

occurred. By the thirtieth day improvement was evident. Many coarse rales were still present in the base of the left lung, but the base of the right lung was almost clear. Tachycardia was present. Bronchoscopic examination by Dr. Clerf revealed inflammation of the whole tracheobronchial tree; it was especially prominent in the lower branch of the left bronchus, which contained thick white exudate. The exudate was again injected into mice. There was a weight loss of 11 Kg. (24 pounds).

When the patient was discharged, forty-three days after the onset of illness, the temperature was normal but the pulse rate hovered between 90 and 110. There were many coarse rales in the lower lobe of the left lung. A roentgenogram showed intensification of the bronchovascular markings, although this was less than before. Density was present in the bases of the lungs, especially in the base of the right lung.

**Laboratory Data.**—Slight secondary anemia was present. Many stippled erythrocytes were present in the early period. Each examination showed a persistent increase in the proportion of polymorphonuclear cells, the percentage being between 80 and 90. Döhle's bodies were present in the neutrophils. Febrile albuminuria was present. Four blood cultures were sterile. No typhoid bacilli were present in the stool. Agglutinins for *B. typhosus*, *Brucella abortus* and *Pasteurella tularensis* were absent. The sputum was examined and cultured seven times. The usual flora of the nasopharynx were present, streptococci predominating. No tubercle bacilli were found by culture or inoculation of guinea pigs. Psittacosis did not develop in any of the mice inoculated with sputum. The blood serum contained no antibodies against the influenza virus.

**Summary.**—Typhoid with bronchitis was strongly suspected until evidence of pneumonia developed on the fourth day. Psittacosis, tularemic pneumonia and military tuberculosis were then suspected until ruled out. A roentgenogram revealed a shadow in the left lung which disappeared a few days later, to be replaced by diffuse shadows in both lungs. Dyspnea, cyanosis, drowsiness, hoarseness, dry cough, abdominal distention, headache, photophobia and pleurisy were prominent symptoms and signs. Visual evidence of laryngitis, tracheitis and bronchitis was obtained. There was a hacking cough, and practically no sputum was raised. Pharyngeal washings were obtained on the eighth day of the disease, but no virus was recovered.

**CASE 10.**—Mrs. T. P., aged 35, a patient of Dr. M. J. Sokoloff, felt tired July 11 and had a shaking chill the next day. Because of fever and malaise she was kept in bed for three days. She improved but on July 15 became worse. There were slight sore throat, conjunctival injection, headache and photophobia. Cough began July 19. It was paroxysmal, dry and racking. Profuse sweats occurred, especially at night. The patient was admitted to the hospital July 21, the tenth day of illness. The temperature was 39.5 C. (103 F.), the pulse rate varied from 100 to 120 and the respiratory rate was about 30 per minute. The tonsils and pharynx were inflamed. There were frequent paroxysms of cough and dyspnea, but no sputum was raised. Cyanosis was present. Signs of atypical pneumonia were present in both lungs. A roentgenogram showed diffuse mottling in both lungs, most dense at the bases. The leukocytes numbered 9,000. Cultures of material obtained from the pharynx showed a mixture of bacteria, chiefly *Streptococcus viridans*, *Micrococcus catarrhalis* and gram-negative bacilli. There were no pneumococci. A blood culture was sterile.

The temperature was irregular and gradually declined until the twenty-second day. Cough, cyanosis and sweating persisted, and the patient was gravely ill. Subsequent leukocyte counts varied between 6,000 and 10,000. The temperature rose again on the twenty-third day and followed an irregular course, averaging 37.8 C. (100.4 F.). Dyspnea, cough, sweating and headache were distressing. On the forty-second day the patient became irrational and complained of severe headache, pain and stiffness of the neck. There was occasional vomiting. I saw her at this time. There were photophobia, inflammation of the pharynx and signs of bilateral pneumonia. The reflexes were variable; Kernig's sign, Babinski's sign and ankle clonus could

be elicited at times. Encephalitis was suspected, and the spinal fluid was examined. It was under 220 mm. of water pressure and contained 270 cells per cubic millimeter and 74 mg. of protein per hundred cubic centimeters. A portion of it was sent refrigerated to Dr. Francis for inoculation tests. The patient was somewhat relieved after the removal of 10 cc. of spinal fluid, and two days later 10 cc. more was removed. This contained 350 cells per cubic millimeter, 78 per cent of which were polymorphonuclear cells. Neither sample contained bacteria. A portion of the second sample was injected intracerebrally into eight mice and into the footpads of three guinea pigs. No virus was isolated. The spinal fluid when examined again a week later contained 290 cells, 91 per cent of which were polymorphonuclears. The patient's condition was grave, and her state varied between coma and lucidity. The reflexes were variable, the pupils reacted sluggishly to light and slight rigidity of the neck persisted. The temperature rose to 40 C. (104 F.), the pulse rate diminished to 70 or 80 and the respiratory rate was 30 per minute. The patient was incontinent of urine and feces. During the next few days she became worse; strabismus, pupillary dilatation and insomnia were present. The ocular fundi were normal. Death occurred on the fifty-fifth day. Permission for postmortem examination was not obtained, but a roentgenogram showed a diffuse haziness and fine mottling of both lungs.

The clinical record of the pulmonary infection in this case closely resembles that in the other cases reported, but, as in one of Scadding's cases, death occurred from meningo-encephalitis. Thus the same problem is raised as pertains to the relation of influenza and the encephalitis which occasionally follows it; namely, are the pulmonary and nervous symptoms caused by one agent or by different agents? No virus was recovered from the nasopharyngeal washings or from the spinal fluid.

The following case was studied at the University of Minnesota hospital in 1934, but the report is included here because of its similarity to the cases of 1938:

**CASE 11.**—A man aged 36 was chilled Oct. 29, 1934. Next day he noted chilly sensations, fever and sweating. On the third day he had a severe chill, sore throat and profuse perspiration, and he went to bed for a day or two. He then returned to work but soon felt chilly and again sought his bed, with a relapse of high fever and generalized aching. He tried to get up but could not because of dyspnea on exertion and severe sharp pain in the left side of the chest. He entered the hospital on the ninth day complaining of difficulty in breathing, sore throat, fever and severe pleuritic pain in the right side. He was slightly cyanotic and had labored breathing and a reddened pharynx. There was slight dulness and a few rales in the lower lobe of the left lung, dulness and bronchial breathing in the base of the right lung and friction sounds in the right axilla. Leukocyte counts varied from 4,000 to 8,000. As the disease progressed there were recurrent attacks of drenching sweats, but there was little or no cough. A few specimens of sputum and material obtained with a swab usually contained bacteria which were predominantly staphylococci. Material aspirated with a needle from the consolidated area of the lung was sterile. The temperature was high, 39.5 C. (103 F.) until the eleventh day, after which it averaged about 38.3 C. (101 F.). It became normal on the twenty-seventh day. The pulse rate varied between 85 and 120 but usually was about 100 per minute. The respiratory rate reached 30 per minute on the twelfth day but was about 22 thereafter in spite of the dyspnea and cyanosis. Blood cultures were sterile. Other serologic tests for typhoid fever, undulant fever and tularemia were negative. A roentgenogram of the patient's chest is shown in figure 10. The tuberculin test was negative during the illness and after recovery. Early in the course of the illness influenza, atypical pneumonia, pulmonary mycotic disease and military tuberculosis were suspected. Later in the course, one physician suggested typhoid with bronchitis. The roentgenologist (Dr. L. G. Rigler) made a diagnosis of capillary pneumonia.

The course of the disease was characterized by cyanosis, dyspnea, pain and a sensation of pressure in the chest, especially on exertion, although tachypnea was not prominent. The patient complained of weakness and perspired profusely until the nineteenth day, after which he improved. In a roentgenogram made five months later the shadows shown in figure 10 were present but diminished in density.

In this case there was evidence of early involvement of the upper part of the respiratory tract, soon followed by diffuse patchy bilateral pneumonia with disseminated areas of density and evidences of consolidation in the bases. Severe pleural pain persisted for nearly two weeks. Dyspnea, cyanosis and profuse sweating, but practically no cough or sputum, were prominent features. The leukocytes were not increased in number, and roentgenograms showed slowly resolving bilateral diffuse pneumonia.

#### SUMMARY

The strikingly similar clinical features of the cases reported suggest that the condition belongs to a disease group not conforming to influenza or the usual form of the common cold but included in an undifferentiated group of infections of the respiratory tract, often called tracheobronchitis, capillary bronchiolitis or bronchopneumonia.

*Pulmonary Symptoms.*—After several days of mild symptoms of hoarseness and sore throat, the temperature rose in each case, reached high levels, persisted with remissions for the duration of the illness and declined by lysis. In the early period in seven cases the pulse rate was slow in proportion to the fever. The temporary remission of symptoms after the first day or two of illness in cases 1, 3, 6, 8, 9 and 10 suggests that the fever may have been biphasic, a characteristic of many diseases caused by filtrable viruses, but accurate data of the first few days is lacking. The fever curves in cases 2, 7 and 9, observed from the first and second days, were not biphasic. Infection seemed to spread rapidly in some cases and more slowly in others until the trachea, bronchi and eventually the lungs were involved in a diffuse, bilateral process which persisted several weeks and was followed by a residuum which lasted several months. There was involvement of much of the smaller bronchiolar system, as manifested by dyspnea and cyanosis in each case, but evidence of consolidation was never striking. Tachypnea was not prominent. In five cases cough was distressing; it was hacking, paroxysmal or continual, but in no case was more than a slight amount of sputum raised. The respiratory rate was increased somewhat in each case but not to the degree expected from the extent of the pneumonic lesion. Cyanosis and dyspnea were noted in all cases. In cases 2 and 11 cough was minimal in spite of widespread pulmonary invasion. The fact that abnormal signs and roentgenographic shadows persisted so long in some cases suggests that the interstitial tissue was severely injured. Severe pleuritis and friction sounds were present in four of the eight cases of serious involvement, and sterile effusion took place in one.

*Nervous and Other Symptoms.*—Next to the symptoms of tracheobronchitis and pneumonia, sweating and drowsiness were most prominent. Sweating was profuse in six of the cases but not striking in case 3. Headache was present in all, but muscle pains were minimal. Photophobia was distressing in five cases. In cases 3 and 10 nervous symptoms were more severe, with stiffness of the neck, photophobia, intense headache, twitching, somnolence and disturbed reflexes sug-

gestive of meningo-encephalitis, and in case 10 the spinal fluid contained several hundred cells per cubic millimeter.

The only symptoms referable to the gastrointestinal tract were constipation, abdominal distention and a heavily coated tongue, which were present in five cases. Loss of weight was conspicuous in four cases. Early in the course of the disease in several cases constitutional symptoms predominated over those arising from the respiratory tract, as in cases 1, 2 and 9, but later the pneumonia attracted most attention.

The fever lasted from ten to forty-three days in the cases of severe involvement but usually about three weeks. Rales and roentgenographic evidence of pulmonary infiltration persisted in some cases for weeks or months afterward.

The routine laboratory data were not unusual. The urine usually gave evidence of transient febrile nephrosis. Slight secondary anemia developed. The initial leukocyte count was about normal, but initial leukopenia was present in two cases. The count usually increased during the course of the fever. The number of polymorphonuclear cells was usually increased relatively and absolutely. Blood cultures never contained bacteria, and agglutinins for other bacillary diseases were absent.

#### THE VIRUS

The failure to isolate a virus in most cases, if one was present, was probably due to the delay before attempts were made or to the weak pathogenicity of the virus for the species of animals which were inoculated. According to British investigators,<sup>3</sup> the probability of obtaining the virus of influenza diminishes rapidly after the third day. These investigators also suggest that when the virus attacks the lungs there is less of it in the upper regions of the respiratory tract.<sup>3</sup> With only two patients of the present series, who had been in close contact, were attempts to obtain a virus made as early as the fourth day of illness. From both patients Dr. Stokes and Dr. Francis obtained an unusual virus, from the nasopharyngeal washings of one and from the blood of the other. It was weakly virulent for mice and caused pneumonia and encephalitis about two weeks after inoculation. It is of interest that a somewhat similar virus was apparently obtained from a series of patients by Francis and Magill.<sup>4</sup> The virus caused meningitis and pneumonitis when inoculated in animals.

Experiments are now under way to determine whether the virus obtained from my patients was (a) actually the cause of the disease, (b) the cause of encephalitis accompanying an infection of the respiratory tract, (c) a commensal unrelated to the disease or (d) a virus accidentally encountered in the animals used in the tests. The last possibility is unlikely, since a similar virus was recovered from the same patients by two investigators working in different cities with different lots of animals. The experimental studies will be reported in detail in a later paper.

#### DIAGNOSIS

As mentioned, in three of the cases in which the signs of pneumonia were delayed, typhoid with tracheobronchitis was suspected because of the suggestive symptoms, signs and laboratory data. Pulmonary

3. Stuart-Harris and his associates,<sup>1</sup> page 104.

4. Francis, Thomas, and Magill, T. P.: An Unidentified Virus Producing Meningitis and Pneumonitis in Experimental Animals, *J. Exper. Med.* 65: 147-160 (Aug.) 1938.



tuberculosis and tularemic pneumonia were suggested in cases 9 and 11, and miliary tuberculosis was suggested in case 10. The clinical descriptions of cases 1, 8, 9 and 11, except for the absence of proof of a biphasic temperature curve, fit well with the clinical description of psittacosis, yet no biologic tests or evidence of contact infection supported this diagnosis. It was more difficult to separate the clinical features from those of influenza or influenzal pneumonia, which several other physicians believed some of the patients to have, yet it was proved that the virus of influenza was not present. Some of the clinical features were more like those of the "febrile catarrhs" described by British observers<sup>1</sup> than those of influenza, and the task now is to determine whether the disease is one member of the undifferentiated group of febrile catarrhs. It seems likely that the disease as discussed here, particularly in the age group dealt with, represents (a) the severe uncomplicated form of an otherwise mild and commonly encountered infection, (b) the visitation of a special form of virus infection in 1938 or (c) several different infections with clinical characteristics in common.

From London in 1937, Scadding<sup>5</sup> reported under the term disseminated focal pneumonia four cases of an unusual pulmonary infection, two of which were strikingly similar to my cases. They were characterized by a gradual onset, malaise, shivering, dyspnea, dry cough, marked sweating, slight leukocytosis and roentgenographic shadows of diffuse pneumonia. The disease lasted three or four weeks, and all patients but one recovered. The patient who died had bulbar encephalitis, which might be significant, considering that there was evidence of encephalitis in two of my patients and that the virus which was recovered from one was pneumonotropic and neurotropic in animals. In Scadding's patient the pulmonary lesion consisted of interstitial inflammation, slight fibrosis of the alveolar walls and edema and hemorrhage in the alveoli, changes which commonly occur with pneumonias caused by filtrable viruses.<sup>6</sup>

That it is permissible to group similar diseases together as probable entities on a clinical basis as I have done here has been shown many times in the past. Most of the infectious diseases were delineated long before their causative agents were discovered. The general behavior of the disease in my cases strongly suggests that the infection was caused by a filtrable virus and was not bacterial in origin, as discussed elsewhere.<sup>7</sup> Its similarities to the virus diseases influenza, colds and psittacosis have been mentioned. If the infection described here can eventually be proved to be an etiologic entity, the matter of naming it will arise. To avoid a name too restrictive or too indefinite it would seem best at present to call it a type of infection of the respiratory tract, perhaps type A, or type A virus pneumonia if it can be proved that the virus was the cause.

#### CONCLUSION

In a series of eight cases of an unusual, uniform, severe infection of the respiratory tract the disease was not caused by the virus of epidemic influenza or psittacosis, nor was it like other commonly described diseases. I was therefore led to regard it as a separate disease entity pending the outcome of further experimental

studies. The infection occurred in adults and began as a mild infection of the respiratory tract; this was followed by severe, diffuse, atypical pneumonia and in two cases by the symptoms of encephalitis. Dyspnea, cyanosis, hoarseness, cough without sputum, drowsiness and profuse sweating were the chief characteristics. The disease lasted several weeks. A filtrable infectious agent recovered from the nasopharynx of one patient and from the blood of another may have been etiologically related to the infection, but the evidence is incomplete. Experiments to clarify this point are under way.

### Clinical Notes, Suggestions and New Instruments

#### ACUTE YELLOW ATROPHY OF THE LIVER FOLLOWING SULFANILAMIDE MEDICATION

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As far as I know, there has been no report of a fatal case of sulfanilamide poisoning in which massive destruction of the liver cells has caused death. The report of such a case, with autopsy, therefore seems to be justified.

#### REPORT OF CASE

*History.*—R. B., a youth aged 18, a university student, seen in the clinic of the Student Health Service Jan. 22, 1938, complained of moderate nausea, vomiting and diarrhea of three days' duration. At the time of his admission he was moderately jaundiced but not cyanosed. He was admitted to the hospital with a diagnosis of acute catarrhal jaundice. After a more complete study in the hospital, the diagnosis was not changed. At this time it was learned that he had been under treatment for gonorrheal urethritis for a little more than two months and that he had been receiving sulfanilamide under the careful supervision of his physician.

His physician later supplied the prescriptions, which called for 80 grains (5.2 Gm.) the first day, 60 grains (4 Gm.) the second, 40 grains (2.6 Gm.) the third, and 20 grains (1.3 Gm.) a day thereafter until 700 grains (140 5 grain tablets, or 45 Gm.) had been taken. A period of rest from sulfanilamide therapy, lasting about two weeks, was then ordered. After this interval, a second series was started but was discontinued after three days because of gastrointestinal symptoms. From statements the patient made it was learned that he had taken sulfanilamide in excess of the prescribed dosage because huge doses controlled the urethral discharge. There was also evidence that he had taken the drug during the prescribed rest period. Unfortunately, more specific information was not obtained before the patient became irrational.

The hospital course was uneventful and afebrile, and the symptoms steadily improved. January 24 he was permitted to leave the hospital to take a final examination, but he returned January 25 with an accentuation of all his initial symptoms.

His initial treatment consisted of a fat-free diet and intravenous administrations of dextrose in saline solution. On the first day he slept almost constantly and had to be awakened for food or medication. About thirty hours after his second admission he became very restless, incoherent, irrational and disoriented. Three hundred cc. of 15 per cent dextrose solution intravenously markedly improved these symptoms. However, on the following day he again became irrational, disoriented and at times violent and noisy. At this time it was noted that the percussion boundaries of the liver were abnormally narrow. A diagnosis of acute yellow atrophy of the liver was made. Intravenous administration of dextrose solution caused little improvement this time. Vomiting became frequent and violent, and the vomitus was bile stained. On the night of the third hospital day he became extremely noisy and violent and had to be restrained. Morphine one-fourth grain (0.016 Gm.) and

5. Scadding, J. G.: Disseminated Focal Pneumonia, *Brit. M. J.* 2: 956-959 (Nov. 13) 1937.

6. Reimann, H. A.: The Pneumonias, Philadelphia, W. B. Saunders Company, 1938, chapter 15.

7. Reimann: The Pneumonias, p. 256.

scopolamine  $\frac{1}{150}$  grain (0.0004 Gm.) were given with only temporary relief; he soon relapsed into the violent stage.

During the next day he remained very restless and at times noisy and violent, needing constant restraint and large doses of sedatives (phenobarbital sodium and sodium bromide). He showed no recognition of his parents. He vomited almost everything he took by mouth, and he was incontinent of urine and feces.

January 29, the fourth hospital day, at 8 a. m., pulmonary edema developed. Four hundred cc. of blood was removed by venesection and he was placed in an oxygen tent. His condition became steadily worse, and he died at 1:55 p. m. His death was respiratory in nature, the heart beats being audible for some time after the cessation of respiration.

The temperature, which had been normal during the first hospital stay, remained so for the first two days of this stay and then rose rapidly and fluctuated between 101.4 and 104.6 F. until death.

**Laboratory Data.**—The Kahn reaction of the blood was negative. The total white blood count on admission was 7,296 with 89 per cent polymorphonuclear neutrophils; on the day before death it was 14,176 with 82 per cent neutrophils. The day before death nonprotein nitrogen of the blood was 33 mg. per hundred cubic centimeters. The icteric index was 133 on admission and 166 the day before death. The urine was essentially normal on admission but showed many casts on the day of death.

**Autopsy.**—This was performed by Dr. M. Pinson Neal approximately three hours after death. In addition to the generalized jaundiced condition of the skin and all the organs, the significant pathologic changes were in the brain, the lungs, the kidneys; the spleen and especially the liver.

The dura mater of the brain was bile stained and excessively wet. The convolutions were rather flat and the sulci filled with fluid. The blood vessels of the meninges were markedly engorged. Otherwise there were no abnormal gross or microscopic manifestations in the brain.

The lungs were wet and boggy; microscopically they showed compensatory emphysema, patchy bronchopneumonia with areas of gray hepatization and others of red hepatization, and rupture of the bronchiolar walls and peribronchiolar hemorrhage.

The spleen weighed 400 Gm. and microscopically showed hyperplastic splenitis.

The kidneys showed nephrosis of undetermined etiology.

The liver weighed 1,200 Gm. and grossly did not appear especially abnormal except for the bile staining. Microscopically it showed a massive breaking up of the liver lobules and liver cords, with separation of the remaining fragments into indiscriminate cell groups. There were areas involving two or more lobules in which not a single liver cell would be recognized as such. The liver cells that could be recognized almost uniformly showed fatty changes, with the cytoplasm containing droplets and globules of fat. Bile pigment was scanty. In some areas the only structures recognized as liver tissue were the bile capillaries. There was very little evidence of inflammatory reaction. The entire picture was one commonly seen in acute yellow atrophy.

#### COMMENT

There was no history or other indication that any drug or possibly toxic substance other than sulfanilamide had been taken by the patient. The initial diagnosis was acute catarrhal jaundice, and this diagnosis was not changed until severe toxic symptoms made their appearance.

As nearly as could be determined, no sulfanilamide was taken after the onset of the symptoms which led to his admission to the hospital. If this is correct, the fatal damage to the liver must have been accomplished by the time the symptoms began. University students, as a group, are surprisingly familiar with sulfanilamide, and unfortunately many regard it as a panacea for any infection. This case seems to give substantiation (if this is needed) to the idea that self medication with this drug is very dangerous, for here liver damage was apparently irreparable by the time any symptoms were recognizable.

University Hospital.

## Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING ARTICLE AND REPORTS.

HOWARD A. CARTER, Secretary.

### THE PHYSIOLOGIC EFFECTS OF ULTRAVIOLET RADIATION

HENRY LAURENS, PH.D., LL.D.

NEW ORLEANS

The physiologic effects of ultraviolet radiation, in contrast to pathology and therapy, are difficult to grasp and to reduce to brief fundamentals.

#### SKIN

Many important effects on the body are mediated by the skin and by changes produced in it. The anti-rachitic effect occurs in the lowermost cells of the horny layer and in the prickle cells of the malpighian layer, while the production of erythema takes place in the basal cells (germinativum) of the malpighian layer and in the corium. The horny, clear and granular layers act as filters. Ergosterol and cholesterol can be activated by ultraviolet rays which pass through the epidermal layer of the skin. Blood in the superficial capillaries absorbs only a small percentage of energy incident on the skin.<sup>1</sup>

The "burn" produced by ultraviolet takes a few hours to appear and the longest wavelength that can produce it is about 3,150 angstroms.<sup>2</sup> The curve representing relative effectiveness of different wavelengths rises to a maximum at 2,967 angstroms, descends to a minimum at 2,800 angstroms, then rises again to a smaller maximum near 2,500-2,450 angstroms and extends to an undetermined shorter wavelength. Blondes are from 40 to 170 per cent more sensitive than brunets, men 20 per cent more sensitive than women. Persons between 20 and 50 are more sensitive than those younger or older. There is an average maximum sensitivity in March-April and in October-November. A person with an unstable nervous system, an overactive thyroid gland, elevated blood pressure or active tuberculosis shows increased sensitivity. The sensitivity increases at the menses—a maximum being reached on the first day of the cycle—and then declines to normal. After the second month of pregnancy the sensitivity markedly increases until the seventh, after which it diminishes somewhat, being still high at term. Increased sensitivity is correlated with thyroid hyperactivity and with increased number of open capillaries in the skin. An acid diet increases sensitivity. Salves exert a protective action, an acid salve less than an alkaline.<sup>3</sup>

The erythema reaction is used as a practical means of evaluating or appraising the ultraviolet output of lamps. So far as known there is no other biologic, physical or chemical reaction which has a similar effectiveness. It is scientifically meaningless and misleading to evaluate therapeutic effectiveness in terms of erythema response unless therapeutic effectiveness very

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1. Laurens, Henry: *Physiological Effects of Radiant Energy*, New York, Chemical Catalog Company, Inc., 1933. *Photochemistry in Medicine: A General Outline*, in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L. I., N. Y., the Biological Laboratory, 1935, vol. 3, p. 277. *Sunlight and Health*, *Scient. Monthly* 42: 312 (April) 1936.

2. An angstrom unit of wavelength is one ten-millionth millimeter.

3. Ellinger, F.: *Biologische Grundlagen der Strahlenbehandlung*, p. 153.

closely follows it, and there is no apparent reason for assuming such a relationship. This can have no meaning unless the sole benefit of radiation therapy arises in some way from the apparent injury as shown by erythema.<sup>4</sup> About nine years ago a request came to the Council for a simple means for determining whether a lamp emits ultraviolet. The Council recommended the erythema test, but it has repeatedly and very specifically stated that the erythema test is not a measure of therapeutic effectiveness. Nevertheless, the use of the erythema reaction is of practical usefulness, since its determination serves to prevent severe burns and to safeguard against the fraudulent sale of lamps deficient in ultraviolet radiation.

Erythema shows the reactions of the "triple response"<sup>5</sup> and depends on the setting free of H-substance.<sup>6</sup> The acidity of the gastric juice increases simultaneously with its beginning.

Care should be used to avoid overexposure. Not only may a painful sunburn result but more deep-seated injury may occur, as indicated by nervousness, apprehensiveness and insomnia. Long continued exposure produces, in some individuals, various cutaneous conditions.

Erythema is followed by pigmentation. Ectodermal pigment is almost exclusively in the basal cells, occurring in the white race in the outer layers only when the skin is well tanned. In Negroes pigment is more abundant in the basal layer but there is also much pigment in the outer, including the horny, layers. The process of adaptation or protection consists in proliferation, cornification, pigmentation and changes in skin cell proteins. The shorter waves are absorbed by the horny layer (about 30 microns thick) and never reach the living cells of the epidermis. The longer waves which penetrate as far as the dermis (50-80 microns) may act on the blood in the papillae. The basal layer pigment, which increases after irradiation with wavelengths shorter than 3,150 angstroms, diminishes the amount of ultraviolet which may reach and penetrate the basal cells and thus protects the dermis from receiving too much energy. The function of skin melanin as a screen against ultraviolet is small in the white race, of more importance in the Negro and is the principal reason for his low sensitivity.<sup>7</sup>

Pigment formation and therapeutic benefit are independent, coordinate phenomena proceeding simultaneously in the same direction. Pigment formation is dependent on individual factors, race, coloring, constitution and body function. It can be used as an index in treatment. It is also a measure of adaptation, since pigment formation, horny layer thickening and chemical alterations of the skin cell proteins run parallel.

#### EYE

The cornea begins to absorb at 3,600 angstroms and transmits to between 2,950 and 3,000 angstroms, and the crystalline lens transmits to 3,060-4,190 angstroms, according to age. The vitreous transmits wavelengths

as short as 2,300 angstroms, with a broad absorption band from 2,500 to 2,800 angstroms. The lens absorbs wavelengths as short as 2,950 angstroms with no ill effects, but shorter wavelengths produce a severe ophthalmia. Sunlight is ordinarily harmless but when the ultraviolet component is increased by reflection, as from sand, water, ice or snow, it produces "snow blindness."<sup>8</sup> Glowing arcs and metals which emit energy shorter than 2,950 angstroms are injurious and special ultraviolet absorbing glasses should be worn. The damage is usually limited to conjunctivitis and blepharitis, with pricking pain and uncomfortable foreign body sensation. Edema and contraction of the lids and corneal erosion may occur. Long continued exposure to intense ultraviolet may produce functional disturbances, such as color scotomas and constriction of the peripheral field. Amblyopia and central scotoma have been noted in "snow blindness." "Eclipse blindness" is due to intense local action of infra-red rays.

It is still a question as to whether intense ultraviolet produces lenticular cataract. Many incline to the view that glass workers' cataract is due to the intense infra-red rays which interfere with the nutritional functions of the ciliary body. It is probable that the higher incidence of cataracts in workers exposed to molten glass and metals is due to increased rate of precipitation of light-denatured protein when the lens is heated above body temperature by exposure to large sources of radiant heat and when low concentrations of calcium, or other substances producing a similar effect, are present.<sup>9</sup>

Claims have been made that some persons can see wavelengths as short as 3,130 angstroms. This is due to excitation of the retina by fluorescent (longer) wavelengths. The aphakic eye sees shorter wavelengths than the normal eye.

#### BLOOD

Long continued darkness produces no marked effect as long as the diet is satisfactory. There is no such thing as "tropical anemia." The number of reds, whites and platelets may be made to increase by appropriate irradiation. Irradiation produces a lowered blood sugar, increased sugar tolerance, increased blood calcium, relative lymphocytosis and eosinophilia. In lymph an increase in protein, a decrease in sugar, an increase in calcium and an increase in cell number have been observed. A leukopenia in peripheral blood and a leukocytosis in splanchic blood has been recorded.

While irradiation with ultraviolet may have some effect on secondary anemia, this is limited and not specific and far less efficient than dietetic and drug treatment.<sup>10</sup>

Intense ultraviolet radiation may result in abnormal white blood cell counts.<sup>11</sup> There is no unequivocal evidence that ultraviolet radiation increases resistance to specific or general infection, although a relationship between sunlight and the general course and character of disease, growth and nutrition has been demonstrated.<sup>12</sup>

4. Brackett, F. S., in Cold Spring Harbor Symposia on Quantitative Biology, 1935, vol. 3, p. 266.

5. Sir Thomas Lewis in 1927 demonstrated that the response of cutaneous vessels to mechanical, electrical, thermal and chemical injury is triple. There is (1) a reddening due to capillary dilatation, (2) a mottled red flare with crenated edges, the result of arteriolar dilatation, and (3) a wheal, due to increased permeability of the minute vessels which permits the escape of fluid, closely resembling plasma in composition, into the tissue spaces.

6. Histamine when introduced into the skin produces a typical triple response, and ultraviolet rays elicit a triple response owing to the local liberation in the skin of histamine or of some closely related substance (H-substance).

7. Laurens: Physiological Effects of Radiant Energy, p. 124; Sunlight and Health.<sup>2</sup>

8. Laurens: Physiological Effects of Radiant Energy, p. 148. Ellinger: Biologische Grundlagen der Strahlenbehandlung, p. 165.

9. Clark, J. H.: Am. J. Physiol. 113: 538 (Nov.) 1935.

10. Laurens: Physiological Effects of Radiant Energy, p. 188; Sunlight and Health.<sup>2</sup> Seyderhelm, Richard: Klin. Wchnschr. 11: 628 (April 9) 1932. Fervers, C.: Med. Klin. 29: 1052 (July 28) 1933; Deutsche Arch. f. klin. Med. 175: 226, 1933; Deutsche med. Wchnschr. 59: 1922 (Dec. 29) 1933.

11. Kennedy, W. P., and MacKay, Ian: J. Physiol. 87: 336 (Sept. 8) 1936; J. Path. & Bact. 44: 701 (May) 1937. Stammers, A. D.: J. Physiol. 78: 335 (June) 1933. de Rudder, B.: Klin. Wchnschr. 13: 167 (Feb. 3) 1934.

12. Laurens: Physiological Effects of Radiant Energy, pp. 232, 259.

## CIRCULATION

There is evidence that sunlight and artificial radiant energy may lower blood pressure, normal and elevated.<sup>13</sup> Certain experimenters, notably Laurens and his co-workers,<sup>13</sup> appear to have demonstrated that the energy emitted by carbon arcs lowers the blood pressure of animals and human beings. Following irradiation intense enough to produce erythema the systolic blood pressure of hypertensive persons may drop an average of 17 mm. (range 2 to 41), the diastolic of 7 mm. (range 2 to 20). The cardiac output (volume per minute) usually increases when the blood pressure is lowered. The precise mechanism involved in the apparent fall in blood pressure obtained under these experimental conditions may possibly be due to factors other than the ultraviolet rays themselves. From a clinical standpoint the claim that ultraviolet rays reduce blood pressure does not appear to have been sufficiently established by the majority of those who have had long experience with natural or artificial heliotherapy to command acceptance. Most of them feel that, while exposure of the entire body to ultraviolet rays may produce some reduction in blood pressure in certain individuals, this reduction cannot be depended on and is too slight and inconstant to be of clinical value.<sup>14</sup>

The lowered blood pressure of persons living in the tropics is the result of the action of a number of characteristics, racial, mode of life, meteorological conditions and their changes and cannot be correlated with the quantity and quality of radiation.

Intense irradiation may markedly accelerate the heart, but this is not specific for ultraviolet. The pulse may become "fuller" and "stronger" during and following a course of irradiations, correlated with increased minute volume.

## METABOLISM

Irradiation of moderate intensity increases endogenous nitrogen metabolism. Residual nitrogen is usually diminished. The excretion of uric acid is said to increase, giving support to the use of ultraviolet in the treatment of gout. Ultraviolet irradiation may double the fat content of the blood, cholesterol increasing by 30 per cent.

The blood sugar of normal men is not influenced to any extent by ultraviolet irradiation, while in some persons with diabetes the blood sugar may be temporarily diminished. The decrease is probably due to increased excretion of insulin. The diminution in blood sugar may be accompanied by increased storage of glycogen in the heart, liver and muscle.<sup>15</sup>

Irradiation of lactating women may increase to some extent the quantity and antirachitic potency of the milk.<sup>16</sup>

The effect of ultraviolet irradiation on respiration is to make it easier, deeper and less frequent. Total ventilation per minute remains constant.<sup>17</sup> It has been generally accepted that basal metabolism is not influenced by ultraviolet irradiation. When an increase in metabolic rate is observed upon insulating the nude body it is due preeminently to the cooling effect of the

moving air. If the air temperature is high with little or no air movement, the chemical heat regulating mechanism is brought into action and the metabolic rate diminishes. Lehmann and Szakáll<sup>18</sup> have demonstrated that brief, intense irradiation, resulting in erythema, leads to an increase in metabolic rate lasting as long as twenty-two hours. Repeated irradiation produces a diminution of between 10 and 15 per cent in basal rate, still demonstrable from three to four weeks after the last irradiation. Parallel with this diminution there is an increased respiratory quotient, from 0.75 to 0.85 to more than 1.0, indicating a preferential combustion of carbohydrate.<sup>19</sup> Ultraviolet irradiation exerts a glycogen storing effect, preventing the lowering of the respiratory quotient after muscular exercise, which lowering is due to glycogen impoverishment.

According to Holtz and Wölpert,<sup>20</sup> ultraviolet irradiation prevents clinical evidence of scurvy in guinea pigs and man due to increased metabolic rate.

## GROWTH

Practically all of the attempts to show effects of light on normal growth processes of man and animals have been negative. Animals will grow as well in darkness as in light if the diet is complete. A rise in the growth curve (height and weight) of children is reported in the spring (March to June), a drop during the hot summer months, a second rise in autumn (September to December) and a depression in winter (December to February).<sup>21</sup> Frank<sup>22</sup> found no apparent correlation with temperature, precipitation or sunlight. Exposure to artificial sources, emitting both short and long waves, produces small increases in height, regarded by Nylin<sup>23</sup> as significant. The increase in weight was at a minimum when the increase in height was maximum, and when there was no irradiation the increase in height was minimum while increase in weight was maximum. Growth curves of Australian infants show that seasonal differences are not large, regular or consistent.<sup>24</sup>

A gain in weight of rabbits living under laboratory conditions and exposed to neon light has been demonstrated.<sup>25</sup> Most of the energy emitted by the lamps was between 5,800 and 7,600 angstroms, the ultraviolet components extending from 3,370 to 3,620 angstroms, the strongest rays being between 3,460 and 3,480 angstroms. The chick requires the ultraviolet as well as the longer portion of the solar spectrum in order to grow normally. Cod liver oil, however, is able to compensate for deficiency in any part of the spectrum.<sup>26</sup> The production and the fertility of eggs are similarly influenced.

Goldblatt and Soames, Steenbock and Black and Hume<sup>27</sup> demonstrated that a growth promoting factor could be induced in rats in vivo. If rats are kept on a diet deficient in growth promoting factors until they cease gaining weight for about four weeks, their livers, fed to other rats, do not possess growth promoting factors. But if, after complete stoppage of growth, the

13. Laurens: *Physiological Effects of Radiant Energy*, p. 168. Johnson, J. R.; Pollock, B. E.; Mayerson, H. S., and Laurens, Henry: *Am. J. Physiol.* **114**: 594 (Feb.) 1936. Laurens, Henry: *Arch. Phys. Therapy* **17**: 199 (April) 1936.

14. Regulations to Govern Advertising of Ultraviolet Generators to the Medical Profession Only, J. A. M. A. **102**: 841-842 (March 17) 1934.

15. Laurens: *Physiological Effects of Radiant Energy*, p. 253. Ellinger: *Strahlenbehandlung*, p. 169.

16. Laurens: *Physiological Effects of Radiant Energy*, p. 256. Ellinger: *Biologische Grundlagen der*

17. Laurens: *Physiologie*, p. 475, 482.

18. Lehmann, G., and Szakáll, A.: *Arbeitsphysiol.* **5**: 278, 1932. Lehmann, G.: *Strahlenbehandlung*, t. 4) 1933.

19. Ellinger: *Strahlenbehandlung*, p. 166. Mayerson: *Syn.* **3**: 308, 1936.

20. Holtz, P.: *Strahlenbehandlung*, p. 182: 164, 1936.

21. Laurens: *Physiological Effects of Radiant Energy*, p. 345.

22. Frank, H.: *Arch. f. Kinderh.* **75**: 1 (Sept.) 1924.

23. Nylin, G.: *Acta. med. Scandinav.*, 1929, supp. 31, p. 1.

24. Clements, F. W.: *M. J. Australia* **1**: 543 (May 6) 1933; **2**: 182 (Aug. 10) 1935; **1**: 647 (May 9) 1936.

25. Laurens: *Physiological Effects of Radiant Energy*, pp. 260, 348.

26. Laurens: *Physiological Effects of Radiant Energy*, pp. 294, 356, 361.

27. Laurens: *Physiological Effects of Radiant Energy*, p. 346.

rats are irradiated with a quartz mercury lamp for a few weeks their livers acquire the property of stimulating for a short while the gain in weight of rats that have ceased growing on a diet deficient in growth promoting factors. These results are due to the activation of vitamin D which is stored in the liver. This was the first actual demonstration that inert provitamin D could be "activated" into vitamin D.

Ultraviolet has no influence on the activity of the thyroid.<sup>28</sup> The goiter producing power of cabbage is reported to be increased by ultraviolet irradiation.

#### MINERAL METABOLISM

Ultraviolet irradiation with wavelengths shorter than 3,130 (particularly 2,967 angstroms) exerts an influence on calcium and phosphorus even when the diet is adequate.<sup>29</sup> But of even greater importance from the standpoint of protection against dietary deficiencies is the action of ultraviolet radiation in rectifying partial lack of the components necessary for proper calcification of bone and teeth.<sup>30</sup>

Ultraviolet irradiation gives rise, from the provitamins in the skin, to vitamin D, the agent which promotes normal calcium anabolism and retention of phosphorus. Therefore it may prevent and cure rickets, adult as well as infantile, promote growth and prevent excessive loss of lime from the body. It apparently does not influence the healing of fractures.<sup>31</sup> It is necessary not only for the development of teeth but for their protection later in life. In dental caries, rickets is only one of several etiologic factors. Enamel is an epithelial tissue, while bone and dentine are connective tissues.<sup>32</sup>

Ultraviolet irradiation may be used in the treatment of infantile tetany, a symptom complex occurring in rickets when the blood calcium is low. The treatment of choice is a combination of a calcium salt (lactate or gluconate), a diet low in phosphate and optimal vitamin D.<sup>33</sup> Latent tetany may become manifest when rachitic infants are irradiated if sufficient calcium is not available, owing to the suddenly increased mobilization and deposition of calcium in the growing bones.

Irradiation of normal rabbits may produce a marked hypertrophy of the external parathyroid which may represent an increased factor of safety to protect the calcium level under conditions of emergency. Keeping chicks in darkness gives rise to a hyperplasia which may be prevented by ultraviolet irradiation. While irradiation of parathyroidectomized animals and man will keep them free from tetany, vitamin D itself is far more efficient.

When an animal is irradiated, its skin, liver, fat and muscle become antirachitically active.<sup>34</sup> Ultraviolet radiation forms vitamin D either in the cells of the living organism or in its foodstuffs. The action of a foodstuff artificially rendered antirachitic by irradiation is qualitatively the same as the action of a naturally occurring

foodstuff containing the antirachitic factor. Slight qualitative differences may exist depending on whether the foodstuff is of animal or vegetable origin.<sup>35</sup> Direct exposure of the skin to ultraviolet rays from the sun or from artificial sources results in the formation of vitamin D within the organism, but the Council cannot recognize statements or implications that vitamin D has all the beneficial effects of exposure to sunshine. Not only have various foodstuffs been irradiated to increase their content of vitamin D but there has been a tendency to add preformed vitamin D to foods.<sup>36</sup> Milk is poor in vitamin D but is an excellent source of calcium and phosphorus. The Council on Foods therefore considers that, of all the common foods available, milk is most suitable as a carrier of vitamin D. The Council has recently made the decision that for the present milk is the only common food which will be considered for acceptance when fortified with vitamin D. One of the methods used to impart antirachitic properties to accepted vitamin D milks is irradiation with ultraviolet shorter than 3,130 angstroms.

Activation depends on the same wavelengths effective directly in the cure and prevention of rickets.

Vitamin D in some way regulates the passage of calcium and phosphorus across the intestinal wall. It exerts its action by raising the blood calcium and/or phosphate. This is associated usually with an increased net absorption from the intestine, though under certain circumstances the bones may provide the calcium and phosphate. The net retention of the animal as a whole is the resultant of two opposing factors: (1) increased absorption from the intestine or diminished excretion to it and (2) increased excretion by the kidney. As the dosage of vitamin D becomes larger, the second factor overtakes the first.

It has been asserted that vitamin D acts through stimulating the parathyroid glands.<sup>37</sup> But the effects of irradiated ergosterol and of parathyroid extract on the plasma phosphatase, on the blood and urine chemistry and on the microscopic appearance and chemical composition of the bones are dissimilar. Parathyroid extract, although it relieves the tetany associated with rickets in infants, fails to induce healing in the rachitic metaphysis and may actually retard it, whereas vitamin D promotes calcification in the metaphysis and in so doing may even temporarily produce hypocalcemia and tetany unless a sufficient amount of calcium is provided. The resemblances between the effects of vitamin D in excess on a diet poor in calcium and those produced by excess of the parathyroid hormone are fortuitous. Similarly the effects of excess vitamin D and of parathyroidectomy on blood calcium are in opposite directions but not connected by any causal relationship.<sup>38</sup> Vitamin D given to rickety animals increases the adsorbable fractions of calcium and the total adsorbable phosphorus. It seems to be the diffusible, adsorbable, calcium phosphorus complex which provides the substance for the calcification of bone. Parathyroid hormone, unlike vitamin D, increases the ion-containing fractions.

28. Laurens: *Physiological Effects of Radiant Energy*, p. 280. Mayer-son, H. S.: *Am. J. Physiol.* **113**: 659 (Nov.) 1935. Webster, Bruce: *Proc. Soc. Exper. Biol. & Med.* **29**: 1070 (June) 1932.

29. Laurens: *Physiological Effects of Radiant Energy*, pp. 257, 261.

30. Laurens: *Physiological Effects of Radiant Energy*, p. 285; *Cold Spring Harbor Symposia on Quantitative Biology*,<sup>1</sup> *Sunlight and Health*,<sup>2</sup> Bunker, J. W., ed.: *Proc. Soc. New England J. Med.* **216**: 165 (Jan. 28) 1937.

31. Sweeney, H. M., and Laurens, Henry: *Effect of Carbon Arc Radiation on Healing of Bone*, *Arch. Surg.* **31**: 395 (Sept.) 1935.

32. Laurens: *Physiological Effects of Radiant Energy*, p. 290; *Cold Spring Harbor Symposia on Quantitative Biology*,<sup>1</sup> *Sunlight and Health*,<sup>2</sup> Schour, Isaac: *Calcium Metabolism and Teeth*, J. A. M. A. **110**: 870 (March 19) 1938.

33. Laurens: *Physiological Effects of Radiant Energy*, p. 334; *Cold Spring Harbor Symposia on Quantitative Biology*,<sup>1</sup> *Sunlight and Health*,<sup>2</sup>

34. Laurens: *Physiological Effects of Radiant Energy*, pp. 347, 389; *Cold Spring Harbor Symposia on Quantitative Biology*,<sup>1</sup> *Sunlight and Health*,<sup>2</sup>

35. *The Present Status of Vitamin D Milk*, J. A. M. A. **108**: 206 (Jan. 16) 1937.

36. Reports of the Council on Foods, J. A. M. A. **108**: 1515 (May 1) 1937, **110**: 511 (Feb. 12) 1938. Vitamin D Milk, Current Comment, *ibid.* **108**: 1894 (May 29) 1937.

37. Taylor, N. B.; Weld, C. B., and Sykes, J. F.: *Proc. Roy. Soc. London* **B 116**: 10 (Sept. 1) 1934; *Brit. J. Exper. Path.* **17**: 104 (April) 1936.

38. Dale, H.; Marble, A., and Marks, H. P.: *Proc. Roy. Soc. London*, **B 111**: 522 (Oct. 1) 1932. Taylor, Weld and Sykes, *ibid.* **116**: 63 (Sept. 1) 1934. Shelling, D. H.: *The Parathyroids in Health and in Disease*, St. Louis, C. V. Mosby Company, 1935, p. 165.

Vitamin D occurs in relatively few foodstuffs, though it can be developed in some by appropriate irradiation. It rarely, if ever, occurs in living plants. Dead plant tissue by insolation may acquire slight potency. In the animal kingdom vitamin D is widespread but is abundant only in fish. Its origin is obscure; some of it may originate by synthesis. Higher animals lack the power to synthesize vitamin D and their requirements are met by ingesting it or by exposing the body surface to sunlight. In all cases, except possibly fish, the ultimate origin of vitamin D is traceable to sterols activated by ultraviolet rays.<sup>39</sup>

#### PHOTODYNAMIC OR OPTICAL SENSITIZATION; PATHOLOGY

It is possible to sensitize living cells, like photographic plates; and thus produce abnormal conditions in which light or luminous rays and longer ultraviolet rays are as active as the shorter ultraviolet.<sup>40</sup> The effective wavelengths are those absorbed by the sensitizer. Sensitization occurs at 4,900-5,800, 3,650-3,130 and 2,500 angstroms. The sensitizers are exogenous, taken in with the food, and endogenous, arising within the organism. Most sensitizing substances are fluorescent, but fluorescence is not the cause. Ultraviolet effects can occur either in the presence or in the absence of oxygen, but the photodynamic effects occur only in its presence. Among photodynamic sensitizers are erythrosin, rose bengal, rhodamin, anthracene derivatives, acridine dyes, methylene blue, quinine, chlorophyll, hypericin and the porphyrins.

Continued and prolonged exposure to sunlight or to the energy of artificial sources containing much ultraviolet may cause systemic disturbances as well as inflammatory and degenerative changes in the skin. The systemic disturbances are not understood, but deaths of infants following short exposure have been reported and severe reactions in adults.<sup>41</sup>

The porphyrins may sometimes sensitize, as in lead poisoning,<sup>42</sup> but even when present in large amounts, as in sulfonal and trional poisoning, they may not. Light sensitivity may even be reduced when porphyrins are present in large quantities, as in hydroa vacciniforme, which would thus seem to be a "climate disease" in which abnormal metabolism of porphyrins is the underlying factor and the combined working of ultraviolet and minor injury (in the form of increased air movement in the spring) the releasing factor. Again, porphyria may not be present in some cases of hydroa vacciniforme and in these instances there may be hypersensitivity to repeated ultraviolet irradiations as well as normal sensitivity. Hydroa vacciniforme is probably a symptom found in numerous conditions.<sup>43</sup> It is further possible that porphyrins play no part in light sensitivity. They may represent products of skin injury and be a result rather than a cause of dermal sensitization. Porphyrinuria may be the result rather than the

cause of the disease, and the excretion of porphyrin is not a constant manifestation of this group of diseases.<sup>44</sup>

Reports on treatment with photodyn and with sulfanilamide indicate that in some persons unpleasant results of photosensitivity may occur.<sup>45</sup>

Urticaria solare may occur after short exposure to sunlight. It is accompanied by immediate and severe erythema, edema and itching. Normal erythema is produced by ultraviolet radiation of wavelengths shorter than 3,150 angstroms. It is a delayed reaction, a "triple response," appearing an hour or more after moderate exposures, and is followed later by pigmentation. Both erythema and pigmentation are independent of oxygen. Urticaria solare manifests itself as a "triple response" and is produced by luminous violet and blue rays (from 3,900 to 5,300 angstroms). It is not followed by pigmentation and is independent of oxygen. Photodynamic "triple response," produced by intradermally injecting rose bengal and hematoporphyrin, is similar in appearance to urticaria solare and is produced by the wavelengths absorbed by the particular sensitizer. The response is immediate. It is followed by pigmentation and does not occur in the absence of oxygen. The mechanism of the urticarial response includes a photochemical reaction not markedly affected by temperature and a thermal reaction greatly modified by changes in temperature. The latter is probably due to the action of the H-like substance on the small vessels of the skin. The photosensitizer is a carotenoid pigment.<sup>46</sup>

The relation of ultraviolet to pellagra is difficult to evaluate.<sup>47</sup> The clinical impression that sunlight is harmful to the pellagrins has been confirmed again by Smith and Ruffin,<sup>48</sup> according to whom the seasonal incidence of pellagra is conditioned by the degree of dietary deficiency and the intensity of the solar radiation. Exposure of a susceptible subject, who has been subsisting on a deficient diet, to the sun's rays precipitates the acute manifestations of pellagra. Pellagrous lesions, however, occur in the absence of sunlight and they may heal in the presence of exposure to direct sunlight or to ultraviolet radiation. Spies<sup>49</sup> suggests that pellagra is a systemic condition which in itself is the real cause of pellagrous dermatitis and not exposure to the rays of the sun. Under conditions sunlight may act as an irritant and precipitate cutaneous lesions. But any kind of irritant may predispose an area to localization of the dermatitis, the absence of which, however, indicates little as to the cure of the disease. Porphyrinuria in pellagra has been described.<sup>50</sup>

Repeated irritation by ultraviolet rays can cause chronic lesions, which may be precancerous, such as

39. Bills, C. E.: *Physiol. Rev.* 15: 52 (Jan.) 1935; in Duggar, B. M.: *Biological Effects of Radiation*, New York, McGraw-Hill Book Company 1: 39, 1936.

40. Laurens: *Physiological Effects of Radiant Energy*, p. 488; Cold Spring Harbor Symposia on Quantitative Biology, 1: Sunlight and Health, Blum, H. F.: *Physiol. Rev.* 12: 23 (Jan.) 1932; Cold Spring Harbor Symposia on Quantitative Biology, 1935, vol. 3, p. 318; Ellinger: *Biologische Grundlagen der Strahlenbehandlung*, p. 190.

41. Greenbaum, S. S.: *Dermatoses Due to Light Sensitization*, Am. J. Dis. Child, 34: 81 (July) 1927; McCormac, H., and McCrea, H. M.: *Brit. M. J.* 1: 693 (April 11) 1925.

42. Blum, H. F.; Allington, H., and West, R. J.: *J. Clin. Investigation* 14: 435 (July) 1935.

43. Laurens: *Physiological Effects of Radiant Energy*, pp. 492, 510. Blum, H. F.: *Ann. Int. Med.* 6: 877 (Jan.) 1933. Ellinger: *Biologische Grundlagen der Strahlenbehandlung*, pp. 198, 203. Blum, Allington and West.

44. Mathews, F. P.: *Photosensitization and the Photodynamic Diseases of Man and the Lower Animals*, Arch. Path. 23: 399 (March) 1937. Blum, Allington and West.

45. Blum, H. F., and Templeton, H. J.: *Sequel to Treatment with Photodyn*, J. A. M. A. 108: 548 (Feb. 13) 1937. Goodman, M. H., and Levy, C. S.: *The Development of a Cutaneous Eruption (Toxicodermatosis)*, ibid. 109: 1009 (Sept. 25) 1937. Schonberg, I. L.: *Purpuric and Scarlatiniform Eruption Following Sulfanilamide*, ibid., p. 1035. Menville, J. G., and Archinard, J. J.: *Skin Eruptions in Patients Receiving Sulfanilamide*, ibid., p. 1008. Frank, L. J.: *Dermatitis from Sulfanilamide*, ibid., p. 1011. Finney, J. O.: *Severe Dermatitis Medicamentosa Following the Administration of Sulfanilamide*, ibid. 109: 1982 (Dec. 11) 1937. Myers, G. B.; Von der Heide, E. C., and Balcerski, Matthew: *Exfoliative Dermatitis Following Sulfanilamide*, ibid., p. 1983. Brunsting, L. A.: *Proc. Staff Meet., Mayo Clin.* 12: 614 (Sept. 29) 1937.

46. Blum, H. F.; Watrous, W. G., and West, R. J.: *Am. J. Physiol.* 113: 350 (Oct.) 1935. Blum, H. F., and West, R. J.: *J. Clin. Investigation* 16: 261 (March) 1937. Blum, Allington and West.

47. Laurens: *Physiological Effects of Radiant Energy*, p. 511; Cold Spring Harbor Symposia on Quantitative Biology, 1935, vol. 3, p. 289.

48. Smith, D. T., and Ruffin, J. M.: *Effect of Sunlight on the Clinical Manifestations of Pellagra*, Arch. Int. Med. 59: 631 (April) 1937.

49. Spies, T. D.: *Relationship of Pellagrous Dermatitis to Sunlight*, Arch. Int. Med. 56: 920 (Nov.) 1935.

50. Bech, W.; Ellinger, P., and Spies, T. D.: *Quart. J. Med.* 6: 305 (July) 1937.



keratosis senilis and xeroderma pigmentosum.<sup>51</sup> It is an open question as to whether xeroderma pigmentosum and skin cancer are really associated with photodynamic action.<sup>52</sup> Roffo<sup>53</sup> believes that in the carcinogenic production of skin cancer by ultraviolet the photodynamic action of cholesterol plays the most important part. The photo-activity is due to the emanation of hydrogen peroxide or similar products. Körbler<sup>54</sup> does not believe that the frequency of skin cancer is due solely to exposure to strong sunlight, although it may result in sensitization due to local increase in porphyrin.<sup>55</sup>

The action of radiation is paradoxical in this regard. If the cells of the basal layer of the skin receive an excessive quantity of radiant energy the two protective processes of cornification and pigmentation become abnormally great (hyperkeratosis and hyperpigmentation) and a third degenerative process starts. People lacking in pigment or much exposed to ultraviolet rays show the highest percentage of skin cancer. The developing neoplasm occurs in the place of greatest proliferation, beginning in a wartlike hyperkeratosis, a precancerous change. A cancer develops from a precancerous lesion not only as a result of a continuation of the initial insult but as a result of any continued trauma. Thus ultraviolet rays do not cause cancer in themselves. They produce characteristic cell changes leading to precancerous lesions in the skin. Any irritation, including continually and excessively applied ultraviolet rays, can cause the precancerous change to become malignant.<sup>56</sup>

#### BACTERIA

Almost all bacteria may be killed or attenuated by ultraviolet rays, but there is considerable variation in the rapidity of their destruction. Those which live in the animal body are most easily affected. Those living free in nature adapt themselves to the action of sunlight and so become relatively resistant to irradiation. Direct sunlight is a powerful germicide for all except a limited number of species like the thio-, or sulfur, bacteria, which utilize sunlight for metabolic processes.<sup>57</sup>

There is general similarity between absorption curves and the reciprocals of curves for incident bactericidal energy. The curves rise rapidly from low levels beyond 3,000 angstroms to a maximum between 2,600 and 2,700 angstroms, then drop to a minimum near 2,400 angstroms and rise again toward a limit beyond the range of experimental observation. The reciprocal of the bactericidal curves matches the absorption curves of certain nucleoprotein derivatives, cytosin, thymine and uracil, more closely than those of various amino acids such as tyrosine, tryptophan or phenylalanine.

The curves expressing bactericidal effect are quite similar for all bacteria but some are more sensitive than others. Beginning with the diphtheria bacillus the effect

increases for *B. coli*, staphylococci and cholera, culminating with typhus. Tubercle bacilli capable of growth disappear at the earliest in two hours and at the latest in five hours when exposed to sunlight.

Bactericidal action is perhaps of only theoretical interest because the action of ultraviolet is effective only in very thin layers, and therefore a therapeutic action can occur only in the most superficial infections and with strong dosage. The use of ultraviolet radiation for the elimination of bacteria in drinking water has received some attention, but insufficient evidence is available to recommend this as a safe process for sterilization. More general use has been made in partial sterilization of water in swimming pools. Here again the evidence is not conclusive. Ultraviolet rays have been used in the diagnosis of ringworm and mycotic infections of the skin. Bacterial cultures may be differentiated by means of fluorescence in ultraviolet rays under certain special conditions.<sup>58</sup>

Wells and his co-workers<sup>59</sup> developed an apparatus to spray organisms into the air and another to centrifuge the air so as to concentrate bacteria and viruses contained in them. They studied the length of time during which droplets of varying sizes containing bacteria remain suspended in the air and tested the viability of floating organisms. Irradiation with a quartz mercury vapor lamp was found to be the most effective measure to sterilize air. Air contaminated with known bacteria was passed at definite distances through the rays. Those which divide in one plane, such as streptococci and pneumococci, were easily destroyed, but the outer layers of cocci which grow in clumps protected the inner ones from the rays. The virus of influenza was easily destroyed. Hart<sup>60</sup> has demonstrated that with bactericidal radiant energy operating room infections are greatly reduced, postoperative temperature in supposedly clean cases is lower and of shorter duration, there is better healing, and the patient has less postoperative discomfort.

Toxins as a rule are not very photostable, while antitoxins are resistant to the action of ultraviolet energy.<sup>61</sup> A comparison of the effects of ultraviolet on vaccine virus and on *Staphylococcus aureus* shows that energy sufficient to inactivate the virus completely kills all the staphylococci. Skin repeatedly exposed to ultraviolet rays is less susceptible to the action of vaccine virus than is nonirradiated skin. The incident energies (between 2,380 and 3,020 angstroms) necessary to kill *Staphylococcus aureus* and to inactivate its homologous bacteriophage run strictly parallel, indicating that in the two instances the same organic structures are absorbing the radiations.<sup>62</sup>

The inactivation of the virus of tobacco mosaic is confined to wavelengths shorter than 3,100 angstroms and the energy required to produce any perceptible effect at this wavelength is more than 100 times that necessary at 2,652 angstroms. The energy values representing 100 per cent killing of *Serratia marescens* are far below the values having any measurable effect on the virus. The wavelength of maximum effect is at 2,652 angstroms. The resistance ratio of virus to bacteria is 200:1. In a comparison of the relative resis-

51. Laurens: Physiological Effects of Radiant Energy, p. 513; Cold Spring Harbor Symposium on Quantitative Biology, 1935, vol. 3, p. 289.

52. Mathews.<sup>44</sup>

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54. Körbler, F.: Strahlentherapie 52:353, 1935.

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Ellinger: ... of Radiant Energy, p. 544.  
Duggar: Bi ... Strahlenbehandlung, p. 138.  
Campbell-Rennell, ... 2:119, 1936. Dreyer, G., and  
1) 1936. ... London S. B. 120:447 (July

58. Pulvertaft, R. J. V.: J. Path. & Bact. 38:355 (May) 1934.

59. Wells, W. F., and Wells, Mildred W.: Air-Borne Infection, J. A. M. A. 107:1698 (Nov. 21), 1805 (Nov. 28) 1936. Wells, W. F., and Brown, H. W.: Am. J. Hyg. 24:407 (Sept.) 1936.

60. Hart, Deryl: J. Thoracic Surg. 6:43 (Oct.) 1936; Operation Room Infections, Arch. Surg. 34:874 (May) 1937; Surgery 1:770 (May) 1937.

61. Laurens: Physiological Effects of Radiant Energy, p. 556.

62. Gates, F. L.: J. Exper. Med. 60:179 (Aug.) 1934.

tance of *B. subtilis* (vegetative and spore forms) and of *B. megatherium* (spore form) as compared with the resistance of *S. marescens* and the virus of tobacco mosaic to ultraviolet irradiation, the curves for spore and vegetative stages are generally conformable. Some spores (*B. megatherium*) are more resistant than others (*B. subtilis*). The resistance of the virus is so much greater than the resistance of spore stages as to be of a different order of magnitude.<sup>63</sup> Exposure to ultraviolet rays inactivates poliomyelitis virus.<sup>64</sup> Diphtheria toxin is destroyed by ultraviolet irradiation and can be sensitized to light. Tetanus toxin keeps less well in light than in the dark and can be shown to be inactivated by ultraviolet rays and by light when photodynamically sensitized.<sup>65</sup>

Both amboceptor and complement can be killed by ultraviolet, the extent of change depending on the albumin content of the serum and the concentration of antibody.<sup>65</sup> Serum complement is much more sensitive to irradiation than the b-lysin of serum or the bactericidal substances of leukocytes.<sup>66</sup> The immunizing power of bacteria, as measured by the agglutinin titer of injected rabbits, decreases considerably when the bacteria are intensively irradiated with ultraviolet rays.<sup>67</sup> Bacteria, bacteriophages and viruses are readily sensitized by photodynamic substances, particularly eosin and methylene blue.<sup>68</sup> Most of the properties of venoms are weakened or completely inactivated by irradiation. The venoms of cobra, daboia and rattlesnake may be photodynamically inactivated.<sup>69</sup>

#### PROTOZOA

The lethal effect on *Paramecium micromultinucleata* increases rapidly for wavelengths shorter than 3,000 angstroms and reaches a maximum at 2,650 angstroms, from which it diminishes for shorter wavelengths.<sup>70</sup> According to Giese and Leighton,<sup>71</sup> 2,654, 2,804 and 3,025 angstroms are about equally effective; 2,537 angstroms is less efficient. Swann and del Rosario<sup>72</sup> found that 2,536 and 2,894 killed *Euglena* readily, while 3,132 and 3,654 had practically no effect.

#### PROTEINS

Irradiation of solutions of proteins produces several effects, including shift in H ion concentration, denaturation, coagulation and increased filtering capacity for ultraviolet rays between 4,000 and 2,670.<sup>73</sup> The coagulation of isoelectric egg albumin solutions on exposure to ultraviolet rays involves three processes: (1) light denaturation of the molecule, (2) a reaction between the light denatured molecule and water, and (3) flocculation on moderate heating of the denatured molecules to form a coagulum.<sup>74</sup> Physiologic applications of the

changes produced in proteins and amino acids by irradiation include the production of erythema, coagulation of lens protein, and biologic oxidations and reductions.

#### FERMENTS

Ferments (enzymes) can be stimulated to increased activity, inhibited or destroyed, depending on the wavelength and intensity of the energy and the duration of exposure.<sup>75</sup>

The ultraviolet absorption spectrum of Northrup's pure crystalline pepsin bears a general resemblance to the absorption spectrums for urease and tyrosine. The absorption band is maximum for 2,750-2,800 angstroms and minimum near 2,500 angstroms. Tests of the rate of inactivation by different bands of ultraviolet, in relation to the absorbed energy, indicate that the destruction spectrum of the enzyme agrees essentially with its absorption spectrum and is similar to that of urease.<sup>76</sup>

The absorption curves of yeast are similar to those of certain enzymes and of nucleoprotein derivatives. The lethal spectrum of yeast in the location of its energy peaks on the wavelength scale resembles the absorption curve of the pyrimidine bases of nucleic acid, cytosin and uracil.<sup>77</sup> Light retards fermentation but ultraviolet rays markedly accelerate it.<sup>78</sup>

Nicotine is darkened and decomposed (oxidized) by ultraviolet rays and loses its vasoconstricting power by destruction of the pyrrolidine ring.<sup>79</sup> Epinephrine solutions are oxidized and lose all normal actions. Appropriate irradiation of solutions of synephrin salts increases their action, while overirradiation destroys their activity.<sup>80</sup> Ultraviolet radiation does not increase the yield of digitalis glucosides.<sup>81</sup>

#### MODE OF ACTION

Physiologic effects have their origin in photochemical reactions produced when the energy is absorbed. The effect is physical, then chemical, and finally biologic.<sup>82</sup>

Photochemical reactions are initiated by a change in electron configuration and velocity. If the incident energy is short enough it will produce vibrations in the electrons, which will be activated. These may then be ejected and the molecule thus ionized; or they may be displaced to an outer orbit, and the atom or molecule activated. Photoelectric phenomena are thus at the basis of all the subsequent reactions. The pathologic action of radiation may be considered as the result of upsetting the electronic configuration so that the proteins attain an isoelectric state and coagulate (aggregation). The nucleus of the cell is the chief point of injury.

When a solution of albumin is irradiated in an atmosphere of nitrogen there arises a reversibly oxidizable substance. The irradiated albumin gives the sulfhydryl reaction and it is suggested that when the skin is irradiated there arises in it a substance of the nature and with the functions of sulfhydryl bodies.<sup>83</sup> Reversible redox systems (glutathione and other SH substances) play important parts in cell function.<sup>84</sup>

63. Duggar, B. M., and Hollaender, A.: *J. Bact.* **27**: 219, 241 (March) 1934.

64. Schultz, E. W.: *J. Pediat.* **1**: 358 (Sept.) 1932. Toomey, J. A.: Inactivation of Poliomyelitis Virus by Ultraviolet Irradiation, *Am. J. Dis. Child.* **53**: 1490 (June) 1937.

65. Laurens: *Physiological Effects of Radiant Energy*, pp. 556, 558. Brooks.<sup>65</sup>

66. Pettersson, A.: *Ztschr. f. Immunitätsforsch. u. exper. Therap.* **75**: 156, 1932.

67. Gärtner, S., and Szathmáry, J.: *Ztschr. f. Immunitätsforsch.* **78**: 256, 1933.

68. Laurens: *Physiological Effects of Radiant Energy*, p. 560. Perdrau, J. R., and Todd, C.: *Proc. Roy. Soc. London, s. B.* **112**: 277, 288 (Feb. 1) 1933. Lin, F. C.: *Proc. Soc. Exper. Biol. & Med.* **33**: 337 (Dec.) 1935. Tung, T.: Photodynamic Action of Methylene Blue on Bacteria, *ibid.* **33**: 328 (Dec.) 1935; **35**: 399 (Dec.) 1936. Tung, T., and Zia, S. H., *ibid.* **36**: 326 (April) 1937.

69. Brooks, in Duggar: *Biological Effects of Radiation* **1**: 341, 1936.

70. Laurens: *Physiological Effects of Radiant Energy*, p. 561.

71. Giese, A. C., and Leighton, P. A.: *J. Gen. Physiol.* **18**: 557 (March) 1935.

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75. Laurens: *Physiological Effects of Radiant Energy*, p. 564. Lyon, in Duggar: *Biological Effects of Radiation* **2**: 1059, 1936. Schomer, *ibid.* **2**: 1151, 1936.

76. Gates, F. L.: *J. Gen. Physiol.* **17**: 797 (July), **18**: 265, 279 (Nov.) 1934.

77. Oster, R. H.: *J. Gen. Physiol.* **18**: 243, 251 (Nov.) 1934. Oster, R. H., and Arnold, W. A., *ibid.* **18**: 351 (Jan.) 1935.

78. Lyon, in Duggar: *Biological Effects of Radiation* **2**: 1068, 1936.

Beckwith, T. D., and Donovick, S. E.: *Proc. Soc. Exper. Biol. & Med.* **35**: 36 (Oct.) 1936.

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82. Laurens: *Physiological Effects of Radiant Energy*, p. 568.

83. Wels, P.: *Arch. f. exper. Path. u. Pharmacol.* **171**: 480, 1933.

84. Holtz, P.: *Arch. f. exper. Path. u. Pharmacol.* **182**: 141, 1936.

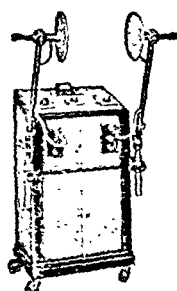
Ultraviolet radiation causes an increase in permeability, liquefaction of the main mass of protoplasm and then coagulation.<sup>85</sup> The primary biologic process is on the large protein molecule and the problem concerns the action on the colloidal systems of the living cell. The effect is a photochemical one, and when there is a photochemical change or decomposition there is a change in the electrical charge of the colloids.<sup>86</sup>

Ultraviolet rays stimulate the basal epidermal cells, arousing them to increased activity and quickened metabolism, so that they set free, in increased amounts, the products of their metabolism. Cellular injury and degeneration, with the consequent setting free of cell decomposition products, may produce beneficial or harmful effects according to the amount set free. The cell products may be (1) the result of increased activity on the part of the basal cell layer of the skin, (2) the result of damage and degeneration or (3) "activated" substances. Substances are given off which, among other things, result in cutaneous hyperemia. These are absorbed subepidermally, are transported away and act on various distant parts of the body. Too great an effect produces harm in normal and in hypersensitive persons. Too intense action, as indicated by an excessive burn, harms or kills the basal cells so that they may give off, if not abnormal chemical derivatives, excessive amounts of normal substances. Ultraviolet irradiation is shock treatment and its value depends on the individual's reaction to it. The dosage must therefore be gaged to the individual.

### LIEBEL-FLARSHEIM ULTRA SHORT WAVE GENERATOR, MODEL SW-400, ACCEPTABLE

Manufacturer: The Liebel-Flarsheim Company, 303 West Third Street, Cincinnati.

The Liebel-Flarsheim SW-400 Ultra Short Wave Generator is recommended for medical use. It is a cabinet model featuring the air-spaced plate technic according to the manufacturer. The electrode arms are counterbalanced, readily adjustable and self retaining without bracing because of frictioned joints. Horizontal and vertical adjustment of the arms is possible. The disks may be raised even higher by hand grips. Two sizes of air-spaced plates, pad and cuff electrodes are included in standard equipment, while a small localizing plate and inductance coil are available accessory equipment. This model may also be used with official electrodes. The unit is finished in walnut and weighs approximately 164 pounds uncrated.



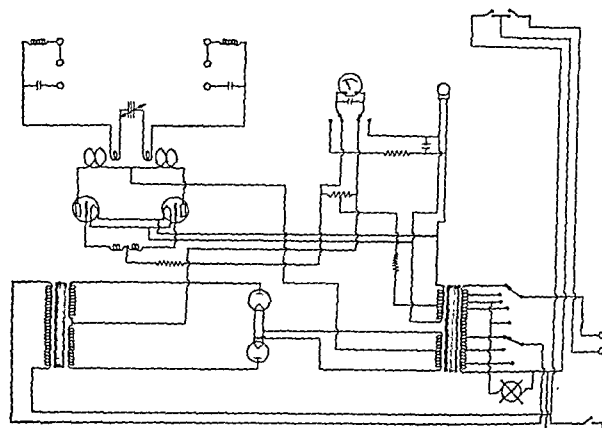
Liebel-Flarsheim  
Ultra Short Wave  
Generator, Model  
SW-400.

A tuned plate, tuned grid circuit is utilized employing two oscillator tubes and two rectifier tubes. The wavelength is approximately 6 meters. The patient's circuit is inductively coupled to the oscillator and a variable condenser is included in the patient's circuit for resonating it with the other circuit. Power input is approximately 1,150 watts. Energy output was measured both by the calorimeter method and by the photoelectric cell and lamp load method, indicating 430 watts respectively. The firm limits its claim to 400 watts output. The temperature rise of the outside of the transformer, after the machine had been operated for two hours at full load, was approximately 38 C. There is a four point power control and an output adjuster. Line filters are to be installed to prevent radio interference.

85. Heilbrunn and Mazia, in Duggar: Biological Effects of Radiation 1: 625, 1936. Ellinger, F.: Strahlentherapie 58: 464, 1937; Nature 138: 1014, 1936.

86. Ellinger: Biologische Grundlagen der Strahlenbehandlung, p. 210. Kartschagin, W. A., and Warschauer, G. S.: Strahlentherapie 40: 174, 1931.

In order to substantiate heating claims made for the unit, the firm submitted the following data: Temperature measurements were made with thermocouples inserted through a cannula into the anterior portion of the thigh to a depth of approximately 2 inches in the quadriceps extensor muscle (for the deep muscle test) and to approximately one-eighth inch for the subcutaneous test. Before the recordings were made, all the thermocouples were carefully checked and the galvanometers calibrated throughout the range of temperatures under consideration.



Schematic diagram.

All treatments were given to the patient's tolerance and a description of the technics employed together with the results of these tests are recorded here:

**Air-Spaced Technic.**—Two small 6 inch disks were applied in a plane parallel to the anterior portion of the thigh. The center of the lower disk was approximately 4 inches above the knee cap, the center of the upper disk approximately 6½ inches above the center of the lower. Both were spaced approximately 1 inch from the patient's skin. Thermocouples were inserted as previously described at the midpoint between the proximal edges of the disks. Temperatures of the skin were recorded at a point on the skin adjacent to the thermocouples. The averages of temperatures for six tests are given in table 1.

**Inductance Cable Technic.**—Six turns of the inductance cable were wrapped round the thigh with approximately 1 inch of turkish toweling beneath for spacing. Three turns were taken

TABLE 1.—Average of Six Observations, Air-Spaced Technic

Deep Muscle		Subcutaneous		Skin	
Initial	Final	Initial	Final	Initial	Final
98.8	104.8	98.5	105.2	93.6	101.5

TABLE 2.—Average of Six Observations, Cable Technic

Deep Muscle		Subcutaneous		Skin	
Initial	Final	Initial	Final	Initial	Final
99.2	104.5	98.7	105.4	95.3	97.5

TABLE 3.—Average of Six Observations, Cuff Technic

Deep Muscle		Subcutaneous		Skin	
Initial	Final	Initial	Final	Initial	Final
98.1	105.1	99.1	105.2	93.6	98.4

high on the thigh, then approximately 4 inches of spacing was allowed and three more turns were taken at that point. The average temperatures for six tests are given in table 2.

**Cuff Technic.**—Two cuff electrodes with two one-fourth inch felt spacers and some additional turkish toweling to a total thickness of about 1½ inches were wrapped round the thigh with about 4 inches space between the proximal edges. The thermocouples were inserted at the midpoint. Temperature rises were recorded as in table 3.

On all these tests treatment was continued for twenty minutes with recordings made at five minute intervals.

The firm submitted tests performed by a qualified investigator as evidence to show the ability of the unit to supply sufficient heat for orificial application. A Chapman electrode was used in the observations specially drilled out so that a thermometer could be passed through and brought into actual contact with the cervical tissue so that the temperature of the cervix, rather than that of the inner portion of the electrode, would be

TABLE 4.—Average Temperatures for Six Sets of Observations, Orificial Technic

Time	Temperature
55	101.5
10	107.0
20	109.5
30	110.0

registered. The orificial applicator was connected to the left hand pad terminal of the machine. For a return path, the large air-spaced plate was connected to the right hand terminal and the plate was placed about 4 inches above the abdominal area. Temperatures were taken at five, ten, twenty and thirty minute intervals. Six such sets of tests were made. The averages are given in table 4.

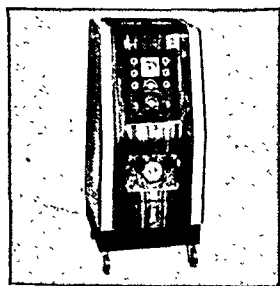
The unit was tried out in a clinic acceptable to the Council and found to give satisfactory service.

In view of the foregoing report, the Council on Physical Therapy voted to accept the Liebel-Flarsheim SW-400 Ultra Short Wave Unit for inclusion in its list of accepted devices

### FISCHER SHORT WAVE APPARATUS, MODEL PC, ACCEPTABLE

Manufacturer: H. G. Fischer & Co., 2324 Wabansia Avenue, Chicago.

The Fischer Short Wave Apparatus, Model PC, is recommended for medical and surgical uses. It is available as either a cabinet or a portable model with either 6 or 12 meter wavelength. The portable unit comes in a keratol covered carrying case with hand grips. This may be slipped into the cabinet housing. The latter comes in two-tone walnut and bird's-eye maple or in plain ivory. Short wave applications may be made with cuff or pad electrodes as well as with the inductance cable.



Fischer Short Wave Apparatus,  
Model PC.

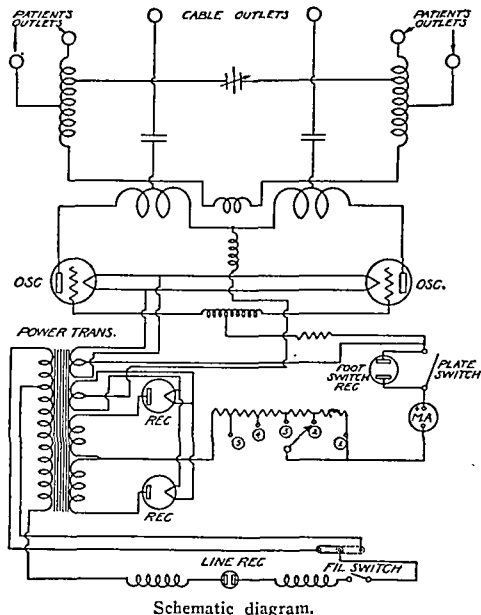
This is a four tube unit with two rectifier tubes and two oscillator tubes. It is wired to force each tube to carry its proper load. Both models have a slightly higher wavelength with cable applications. The 6 meter unit requires a power input of approximately 650 watts and has an approximate output of 260 watts as measured by the photometric method. The transformer temperature when the unit is operated at full load is approximately 182 F.

Cabinet temperatures taken at the top and the base of the cabinet are 151 and 115 F. respectively.

A power input of approximately 750 watts is required with the 12 meter apparatus. With this unit the power output as measured by lamp load and the photometric cell method is approximately 300 watts. The transformer temperature of the apparatus when operated at full load is approximately 180 F. Temperature rises inside the cabinet at top and bottom respectively are 150 and 113 F. Radio interference has been reduced to a minimum by the use of radio frequency chokes in the power supply circuit.

In order to substantiate heating claims made for the unit, the manufacturer submitted tests performed by a reliable investigator. Four male subjects whose weight ranged from 145 to

210 pounds were used in making twenty-four tests. The technical procedure for making the tests was that outlined by the Council on Physical Therapy. The results are given in the accompanying tables.



Schematic diagram.

The following technics were used in obtaining the results recorded:

(a) Cuffs  $3\frac{3}{4}$  by 32 inches and  $3\frac{1}{4}$  by 24 inches. Three-fourths inch spacing consisting of one layer of toweling. Plate current varied from 300 to 320 milliamperes. Cuffs  $7\frac{1}{2}$  inches center to center and equidistant from cannula.

(b) Four turns of cable around the thigh. Varied from 7 to 8 inches over all. Three-fourths inch spacing consisting of one layer of one-fourth inch felt and one layer of toweling. Plate current varied from 290 to 380 milliamperes.

#### The Fischer 6 Meter Short Wave Apparatus, Model PC

(a) Average of six observations, cuff technic:			
Deep Muscle		Oral	
Initial	Final	Initial	Final
99.5	106.8	98.3	98.8
(b) Average of six observations, inductance coil technic:			
Deep Muscle		Oral	
Initial	Final	Initial	Final
99.4	107.7	98.3	98.8

#### The Fischer 12 Meter Short Wave Apparatus, Model PC

(c) Average of six observations, cuff technic:			
Deep Muscle		Oral	
Initial	Final	Initial	Final
99.5	108.0	98.4	98.9
(d) Average of six observations, inductance coil technic:			
Deep Muscle		Oral	
Initial	Final	Initial	Final
99.5	107.5	98.7	99.0

(c) Two cuffs,  $3\frac{1}{2}$  by 24 inches and 4 by 32 inches. Three-fourths inch spacing consisting of one layer of one-fourth inch felt and one layer of toweling. Plate current varied from 280 to 325 milliamperes. Cuffs varied from 7 to  $8\frac{1}{2}$  inches center to center and were equidistant from the cannula.

(d) Four turns of the cable about the thigh. Varied from 7 to 8 inches over all. Three-fourths inch spacing consisting of one layer of one-fourth inch felt and one layer of toweling. Plate current varied from 260 to 200 milliamperes.

Both models were investigated clinically by a competent physician, who reported that they rendered satisfactory service.

In view of the foregoing report, the Council on Physical Therapy voted to include the Fischer Short Wave Apparatus, Model PC, in its list of accepted devices.

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SATURDAY, DECEMBER 24, 1938

## CORONARY OCCLUSION WITHOUT PAIN

In a recent communication Gorham and Martin<sup>1</sup> point out that the incidence of coronary occlusion and cardiac infarction without pain is much higher than has been heretofore appreciated. They have analyzed 100 cases in which necropsy was performed. Forty-two of these patients suffered a fatal attack which was not accompanied by pain, while fifty-eight complained of pain of varying location, intensity and duration. Coronary occlusion was the primary cause of death in eighty of the cases, definitely contributory in fifteen and probable in five. At necropsy gross infarction of the myocardium measuring more than 1 cc. in diameter was found in every case, as well as sclerotic changes in the coronary arteries. Nineteen per cent of the patients in the group without pain gave a history of definite anginal pain previous to the final attack. A comparison of the two groups brought out that patients in the group without pain tended to be older than those in the group with pain, that the peak of mortality for the males is a decade earlier than for the females, that a history of preceding attacks of anginal pain and of hypertension is less common, that dyspnea is a prominent symptom and that a pericardial friction rub is rarely heard. Old infarctions, with absence of actual thrombosis and pericarditis, are more frequent. Pain was present in every one of fifteen patients who showed a combination of actual thrombosis of the coronary artery and acute infarction. However, a combination of fibrotic narrowing of a coronary artery without actual thrombosis, plus an old infarction and absence of pericarditis, was not accompanied by pain in twelve of seventeen cases (70 per cent). Wearn reported 53 per cent, Davis 40 per cent, Bruenn, Turner and Levy 61 per cent and Saphir and his associates 38 per cent of cases in which there was coronary occlusion and infarction without a preceding attack of pain. Kudrin found fifty cases with a history of anginal pain among 500 instances of sclerosis of the coronary artery found by him post mortem.

1. Gorham, L. W., and Martin, S. J.: Coronary Occlusion With and Without Pain: Analysis of 100 Cases in Which Autopsy was Done with Reference to the Tension Factor in Cardiac Pain, *Arch. Int. Med.* 62: 821 (Nov.) 1938.

Anginal symptoms were present in only eleven of thirty-four cases of coronary stenosis and in fifteen of thirty-six cases of coronary occlusion. Boyd and Werblow<sup>2</sup> believe that painless coronary thrombosis must be fairly common, since one third of their 127 patients with proved coronary thrombosis did not manifest pain. A somewhat dissenting opinion is expressed by Kennedy,<sup>3</sup> who found in a recent study of 200 necropsies in cases of myocardial infarction that classic pain was present in 91 per cent of the recent and 64 per cent of the old cases. It appears from numerous observations that while the presence of actual occlusion of the coronary artery favored the occurrence of pain in about two thirds of the cases, the reverse is not true. There must therefore exist still another factor besides thrombosis on which the initiation of cardiac pain depends. Gorham and Martin's study suggests that painless coronary occlusion represents a more gradually developing pathologic process in which the progressive narrowing of the artery results from fibrosis rather than from actual thrombosis.

The cause of initiation of cardiac pain has been the subject of much speculation and in recent years of extensive experimental study. Allbutt's and Wenckebach's mechanical theory of the aortic origin of pain has been largely displaced by Lewis's conception of a chemical origin of pain originating in the heart muscle. His observations on pain produced in a limb which was exercised while its blood supply was arrested led him to believe that cardiac pain was dependent on the myocardial ischemia resulting from the impairment of the coronary circulation. This led to the development in the heart muscle of an unknown chemical "P substance" which acts as a pain producing stimulus to the nerve endings. Herrick explained the absence of pain in some cases in the presence of an extreme grade of ischemia by assuming that in such areas there existed a destruction of vessels, nerves and functioning muscle so that a painful response to the new obstruction was lacking. In recently reported experiments Martin and Gorham<sup>4</sup> attempt to prove that the mechanical factor of tension within the coronary arteries may be of major significance in the production of pain. These authors inquire as to why the receptors of pain sensations (afferent sympathetic fibers) in the coronary arteries, like pain receptors elsewhere in the body, may not be subject to mechanical as well as chemical stimulation. Following the technic and the criteria of Lueth and Sutton, they demonstrated that a typical pain response can be elicited in a dog when tridirectional tension is applied to a coronary vessel in such a manner as to cause no change in blood flow. With this procedure the chemical factors caused by impaired coronary blood flow are completely eliminated. The authors conclude that ten-

2. Boyd, L. J., and Werblow, S. C.: Coronary Thrombosis Without Pain, *Am. J. M. Sc.* 104: 814 (Dec.) 1937.

3. Kennedy, J. A.: The Incidence of Myocardial Infarction Without Pain in 200 Autopsied Cases, *Am. Heart J.* 14: 703 (Dec.) 1937.

4. Martin, S. J., and Gorham, L. W.: Cardiac Pain: An Experimental Study with Reference to the Tension Factor, *Arch. Int. Med.* 62: 840 (Nov.) 1938.

sion alone on the coronary arteries in dogs may serve as an adequate stimulation for the initiation of cardiac pain.

Obviously all discussion of cardiac pain must, at least for the present, remain somewhat speculative, in view of the fact that the mechanisms of the production of pain are as yet but little understood.

### HERBAL TREATMENT OF DIABETES

Notwithstanding the tremendous publicity given to the modern scientific treatment of diabetes, reports continue to appear of deaths following discontinuance of insulin by some patient on the recommendation of osteopaths, Christian science healers, naturopaths and herbalists. The London *Lancet* (Oct. 8, 1938, p. 849) recently noted such a case:

During an inquest last week it was alleged that a herbalist had dissuaded a diabetic patient from receiving insulin treatment. The deceased, a young man of 22, last year developed symptoms which were attributed to diabetes. A doctor prescribed insulin injections and four or five were given. Afterwards the young man's father, according to his own evidence at the inquest, decided that dietetic treatment would meet the case. Having been treated both by a registered medical practitioner and an osteopath, the patient went to Mr. T. H. Wilbraham of Ellesmere-road, Altrincham, a herbalist. The father told the coroner that Mr. Wilbraham said he specialized in the treatment of diabetics and strongly disapproved the use of insulin. The young man's condition, said his father, improved until the beginning of last August. On Sept. 4th a doctor ordered his immediate removal to hospital. He was admitted to a Stockport hospital in a state of coma and died next day. Dr. W. H. Grace, who gave evidence on the pathological side of the case, attributed the coma to the exclusion of insulin. On behalf of Mr. Wilbraham the father was asked in cross-examination whether Mr. Wilbraham had not suggested that, during his treatment, a doctor should administer the correct insulin injections. This the father denied. The coroner's jury returned a verdict of manslaughter, and Mr. Wilbraham was committed for trial.

Not long ago an article advocating a new herb for the oral, non-insulin treatment of diabetes mellitus appeared in the *Canadian Medical Association Journal* (July 1938, p. 32). Gobind Lal, Hearst science editor, among others, called attention to the article, and thus it was relayed to the general public. Several herbs are known to contain hypoglycemic principles. However, no one with the simplest understanding of the physiology of the pancreas and pathology of diabetes mellitus would ever consider any of them as adequate substitutes for insulin. Incidentally, the article in the Canadian journal referred only to some preliminary experiments on animals and observation of the effects in one human case.

Innumerable investigators continue to seek an oral preparation which will suitably control diabetes. The experiments thus far have not given much promise of success. In the meantime, therefore, physicians may well emphasize constantly the specificity of insulin in the successful management of diabetes. Successful management of the disease with insulin means prolongation of life. Until some preparation equal or superior to insulin is developed, patients must be made to

realize the dangers of using any other remedy, particularly any herbal preparation which may be advocated, usually on the basis of avoiding hypodermic injections. Many such preparations have come to the attention of the various Bureaus and Councils of the American Medical Association. The Council on Pharmacy and Chemistry has declared some of them unacceptable,<sup>1</sup> and the Bureau of Investigation has reported an extensive list of unsuccessful remedies for this condition.<sup>2</sup> Premature publication of experimental results may menace the lives of human beings. When such items are exploited by the press, people are led to abandon specific treatment which to them may mean the difference between life and death. While all may earnestly hope for the day when a successful oral treatment of diabetes will become available, today we must exert every effort to educate the victims of this disease in the dangers of abandoning life-saving insulin preparations.

### DESTRUCTION OF VITAMIN C IN THE GASTROINTESTINAL TRACT

Sufficient gastrointestinal fermentation of vitamin C may take place in certain persons to cause vitamin deficiency. In connection with this assertion Kendall and Chinn<sup>1</sup> of Northwestern University Medical School suggest a plausible method for the dietary control of this excessive fermentation. The effect of gastrointestinal bacteria on vitamin C (or on synthetic ascorbic acid) has been the subject of much experimental study during recent years. Stepp and Schröder,<sup>2</sup> for example, tested eight strains of *Bacillus coli* for their destructive action and found but one strain that would utilize ascorbic acid in vitro. Novotel'nov and Vodova<sup>3</sup> tested most of the known species of gastrointestinal bacteria and found none that would destroy vitamin C. The general conclusion<sup>4</sup> drawn from the accumulated evidence is that ability to use ascorbic acid is occasionally shown by certain individuals of known bacterial species but is not a common property of any known species. Kendall and Chinn, however, call attention to the

1. Since the time of its organization in 1905, the Council on Pharmacy and Chemistry has reported unfavorably on a number of proprietary medicinal articles which have been proposed for use in the treatment of diabetes. A list of these preparations follows: Cellasin, Filudine, Globeol, Succinolac, Hemo-Therapin, Chlorax, Intarvin, Diabesan, Blueberry Leaf Extract, Recresal, Sulfobetol, Eubetin, Tryptoferm, Pancresal Tablets, Imbak Preparations and Anticomane.

2. The Bureau has publicized hundreds of fake diabetes "cures" and "treatments." Dr. Arthur J. Cramp, in *Hygeia* for October 1935, discussed or mentioned the following: Amber-ita, Banbar, Bauer's Antibioticum, Beto, Marie Carr Fraud, Diabesan, Dia-Bet, Diabeticine, Diabetol, Diabetylin, Diaplex, Dill's Diabetic Mixture, Eksip, Expurgo (Sanol) Anti-Diabetes, Flowering Herb, Insoloid, Jamun Compound, Kaadt Treatment, Kelpe'koe, Korectone, Letone, Lifcore, Melatol, Mel-Tex, Pancretone, Photo-Synthetic Tea, Sal-Sano, Sanborn Treatment, Scheidemann's Shrub Remedy, Uvursin, Vinculin, Vindor Diabetic Wine, Warner's Safe Diabetes Remedy and Winroy. Since the appearance of that article, the Bureau of Investigation has published reports on the following related subjects which are not mentioned in the article: Linden Ray Emerick, M.D., Carr Laboratories, Sanovapor Dexene, Special Treatment for Diabetes [sic], Diatone and Delatol Laboratories.

1. Kendall, Arthur Isaac, and Chinn, Herman: *J. Infect. Dis.* **62**: 330 (May-June) 1938.

2. Stepp, W., and Schröder, H.: *Klin. Wchnschr.* **14**: 147 (Feb. 2) 1935.

3. Novotel'nov, N. V., and Vodova, V. A.: *Proc. Sci. Inst. Vitamin Research U. S. S. R.* **2**: 81 (No. 1) 1937; abstr., *Chem. Abstr.* **31**: 8615 (Nov. 20) 1937.

4. von Gagy, J.: *Klin. Wchnschr.* **15**: 190 (Feb. 8) 1936. von Gagy, J., and Ujsághy, P., *ibid.* **15**: 793 (May 30) 1936.



fact that routine plating methods used by previous investigators are not well designed to show the real frequency of vitaminolytic variants; so they devised an enrichment method, an ascorbic acid broth in which vitamin C fermenters tend to overgrow nonfermenting variants. After twenty-four hours' growth in this differential medium, ordinary plating methods are used.

The Chicago bacteriologists applied this differential technic to a bacteriologic study of stomach contents from patients with pernicious anemia and from patients with achlorhydria, to feces from babies and adults and to the intestinal contents of guinea pigs. Thirty-four ascorbic acid fermenting strains were isolated, almost every sample tested yielding positive results. Twenty-two of these vitaminolytic strains were classified as *Mucosus capsulatus*. Within twelve hours a strongly lytic strain may destroy approximately 50 per cent of the vitamin C present in their routine ascorbic acid broth and fully 97.5 per cent by the end of twenty hours. This destruction occurs under both aerobic and anaerobic conditions.

The Northwestern University bacteriologists found that the presence of even small amounts of dextrose (and by inference other simple, readily fermentable sugars) definitely postpones decomposition of ascorbic acid until all the dextrose is hydrolyzed. Since citrus fruits are rich in simple sugars, it would seem probable that these sugars will deflect microbic attack on vitamin C as long as the sugars are present in the digestive tract. Whether or not cane sugar added to fruit will further inhibit vitamin destruction was not tested.

## Current Comment

### TUBERCULOSIS IN YOUNG WOMEN

Why should tuberculosis be taking a relatively heavier toll from young women than from any other group of the population? Information on this question was obtained by the National Tuberculosis Association<sup>1</sup> through investigation of the homes of all girls and women between 15 and 25 who died from tuberculosis in New York City in 1929 and of a similar group who died in Detroit during 1930. In New York City the number investigated was 678 and in Detroit 180. One of the most striking facts brought out by the study was the relative similarity of the main observations in the two cities in spite of the fact that the tuberculosis death rate among young women was only 83 per hundred thousand in New York City as compared with 138 per hundred thousand in Detroit. The investigation allowed several specific conclusions, among which were that both cities have an appreciable Negro problem, tuberculosis takes the highest toll in late adolescence and early adult life rather than school age, and race, nativity, residence and immigration seem to have no essential relation to the problem, although the variations in racial susceptibility noted in other groups was

also evident here. There was no evidence of greater mortality among uneducated than among educated girls. There was no reason to believe that industrialization or any specific occupation was responsible for the unequal ratio between the tuberculosis death rates of this group and others or that increased tuberculosis mortality among young women is due to insufficient clothing, diet, lack of sleep or unusual recreational habits. Although it could not be statistically proved, it is believed that the psychic and physical changes of adolescence and early adult life cause young women to be unusually susceptible to tuberculosis and constitute the fundamental reasons for the high mortality rates which they sustain. A distinct relationship between pregnancy and the onset of tuberculosis was shown. Finally, the report concluded that the symptoms of tuberculosis were often recognized late with consequent delay in securing medical advice and treatment, and that clinic facilities were not widely used or sanatorium care given sufficiently early or consistently. As a result of this study the author believes that the excess tuberculosis in young women is essentially biologic rather than environmental in origin.

### INCIDENCE OF MOTTLED ENAMEL AFTER CHANGE OF WATER SUPPLY

The presence of fluoride in drinking water is responsible for the occurrence of "mottled enamel." Fluoride affects the unerupted tooth rather than the fully developed tooth, thus accounting for the prevalence of the condition in restricted age groups even though all use the same source of drinking water. The incidence of mottled enamel in a locality prominent in the history of this dental condition, Bauxite, Ark., has recently been redetermined<sup>1</sup> ten years after a change in the common water supply from one containing significant amounts of fluoride to one free from this substance. At the time of the first Public Health Service survey in Bauxite, in 1928, 44 per cent of all school children between the ages of 5 and 18 years showed definite evidence of mottled enamel and sixty-one of sixty-three children of this age who were born in Bauxite and had always lived there were affected. The occurrence of dental fluorosis in children of this age group was attributed directly to the fact that the city water supply from 1909 to the date of the early survey was obtained from a deep well the water of which contained significant amounts of fluoride. In 1928 the use of the deep well was discontinued, filtered river water being employed instead. The fluoride content of the latter was found to be negligible. Early this year a new survey of the incidence of mottled enamel in Bauxite school children was made. A decrease in the occurrence of the condition to practically zero was found in those children whose teeth had erupted since the water supply had been changed. These observations are the second recorded successful instance in the United States in which it has been shown that the changing of a water supply from one containing fluoride to one free from this substance can bring about a complete eradication of endemic mottled enamel.

1. Nicholson, Edna E.: Tuberculosis Among Young Women, Social Research Series of National Tuberculosis Association No. 7, 1938.

1. Dean, H. T.; McKay, F. S., Elvove, Elias: Mottled Enamel Survey of Bauxite, Ark., Ten Years After a Change in the Common Water Supply, Pub. Health Rep. 53: 1736 (Sept. 30) 1938.

# ORGANIZATION SECTION

## THE SPECIAL GRAND JURY RETURNS INDICTMENTS

The Special Federal Grand Jury, which has been conducting an investigation in Washington, D. C., for more than two months, returned indictments, December 20, charging violation of the Anti-Trust Laws against the American Medical Association, the Medical Society of the District of Columbia, the Harris County (Texas) Medical Society, the Washington (D. C.) Academy of Surgery, and twenty-one individuals. The specific test of applicability of the anti-trust statutes to the medical profession was based on the District of Columbia cooperative, known as Group Health Association, Inc. The indictment charged the defendants with conspiring to "hinder and obstruct Group Health Association, Inc., in obtaining access to hospital facilities for its members." The indictment was signed by Thurman Arnold, Assistant Attorney General of the United States, David A. Pine, United States Attorney for the District of Columbia, and John Henry Lewin, Allan Hart, Douglas B. Maggs and Grant W. Kelleher, special assistants to the Attorney General. According to United Press reports, the indictment charged the defendants with "having combined and conspired together for the purpose of restraining trade in the District of Columbia"; that is to say: "(1) for the purpose of restraining Group Health Association, Inc., in its business of arranging for the provision of medical care and hospitalization to its members and their dependents on a risk-sharing prepayment basis, (2) for the purpose of restraining the members of Group Health Association, Inc. [in Washington], in obtaining, by cooperative efforts, adequate medical care for themselves and their dependents from doctors engaged in group medical practice on a risk-sharing prepayment basis, (3) for the purpose of restraining the doctors serving on the medical staff of said Group Health Association, Inc., in the pursuit of their calling, (4) for the purpose of restraining doctors (not on the medical staff of Group

Health Association, Inc.) practicing in the District of Columbia, including the doctors so practicing who are made defendants herein, in the pursuit of their callings, (5) for the purpose of restraining the Washington hospitals in the business of operating such hospitals.

"In so doing, defendants have then and there engaged in an unlawful combination and conspiracy in restraint of trade in and of the District of Columbia, in violation of Section III of the Act of Congress on June 2, 1890, known as the Sherman Anti-Trust Act."

"Plans, understandings and agreements to accomplish the unlawful business herein above described were proposed, discussed and adopted at such meetings" (the indictment apparently refers here to meetings of the Medical Society of the District of Columbia, at which the Group Health Association, Inc., was discussed).

In announcing the decision of the government to press for criminal indictments, Mr. Arnold is reported to have said that such procedures seemed the only method to resolve the issues raised in the situation. The individuals indicted include Dr. Olin West, secretary and general manager of the American Medical Association, Dr. Morris Fishbein, editor of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Dr. Rosco G. Leland, director of the Bureau of Medical Economics, Dr. William C. Woodward, director of the Bureau of Legal Medicine and Legislation, and Dr. William D. Cutter, secretary of the Council on Medical Education and Hospitals, all from the headquarters of the Association in Chicago. The following remaining individuals named in the indictments are all from the District of Columbia: Drs. Arthur C. Christie, Coursen B. Conklin, James Bayard Gregg Custis, Thomas A. Groover, Robert A. Hooe, Leon A. Martel, Thomas E. Mattingly, Francis X. McGovern, Thomas E. Neill, Edward H. Reede, William M. Sprigg, William J. Stanton, John O. Warfield Jr., Prentiss Willson, Wallace M. Yater and Joseph R. Young.

## THE PACIFIC COAST ECONOMIC CONFERENCE

The second Pacific Coast conference was held at Portland, Ore., December 4. The meeting was attended by representatives from California, Idaho, Oregon and Washington.

Organized medicine now finds itself faced with so many problems and so much to consider that every possible method of reaching solutions must be utilized. With expectation that the Pacific states might help one another in solution of similar problems, the first Pacific Coast conference was called in San Francisco last February. Those in attendance were impressed with the unity of needs of organized medicine in the Pacific region and therefore anticipated an even more valuable conference when Charles Sears, president of the Oregon State Medical Society, invited representatives from Arizona, California, Idaho, Nevada and Washington to meet with the Oregon group in Portland.

Such similarity of problems and so many matters of regional interest were brought to light, and so much information was given on activities of neighboring state organizations, that the conference was established as a permanent organization. Henceforth it is to be known as the Pacific States Medical Executives' Conference and will draw its personnel from those in positions

of responsibility in state associations of California, Idaho, Montana, Nevada, Oregon, Utah, Washington and Wyoming. The next meeting is scheduled for Seattle.

The conference is not to be a legislative body but is intended only to be mutually advisory and a means of trading ideas for solution of problems confronting state organizations of the Pacific region.

The most interesting feature of the Portland meeting was the discussion by members of the California delegation of plans to be brought before a special meeting of the California house of delegates, December 17. Owing to the importance of the proposals revealed and the fact that they had not yet been officially acted on, the California participants requested that their discussion remain unreported. Official report of the coming meeting of the California house of delegates will reveal the extensive nature of the far-reaching plans proposed for California. Those in attendance at the Portland conference appreciated the opportunity of this preview afforded by the California delegation, and the many questions brought out were evidence of the interest evoked. Next in interest was the discussion of several federal activities in regard to medical care. The first discussion on

these matters came from V. W. Spickard, Seattle, who warned of the attempts of welfare and social departments to obtain administrative authority over funds now appropriated and probably to be appropriated by the federal government in the coming legislative session. It was his thought that such funds, appropriated for furthering health activities, should be administered as far as possible through state boards of health or state health departments. It was suggested that the advantages of such power might be misused by such departments of health as were not in close contact with the aims and purposes of organized medicine. This objection, however, was answered when it was brought out that as a general principle state departments of health are usually more closely attuned to the ideals of organized medicine than are departments of social welfare. All representatives at the conference saw the importance of this suggestion, and a resolution was passed to the effect that each state organization make vigorous effort to have federal funds for health activities controlled by state departments of health rather than by departments of welfare.

As a portion of the discussion on federal funds, the proposals of the federal farm security plans for medical care were discussed. The consensus was that it is possible to handle this type of work only through county and local societies. Since it has been extremely difficult to get the federal administrator to accept any responsibility for statewide plans, it was brought out that the local societies should be cautioned against accepting fee schedules too small to provide adequate service. Fear was expressed that acceptance by one county society of very small fees might be used to influence other societies toward impractical contracts.

The afternoon session of the conference brought out a discussion of methods of publicizing organization policies and activities to both the medical profession and the lay public. The meeting was closed after discussion by Martzloff of Oregon and Dudley of Washington on malpractice insurance. Oregon's

plan of granting monopoly to one insurance carrier was explained in some detail by Martzloff. He stated that cost of insurance to members of the Oregon State Medical Society had by this plan been reduced to unbelievably low figures, suits had markedly diminished in number, and splendid cooperation had been obtained between the insurer and the society. Dudley explained the workings of the Washington state medical defense fund. Those in attendance at the meeting were Charles Sears, president of the Oregon State Medical Society, chairman of the conference; John Fitzgibbon, Portland, Ore., delegate to the American Medical Association; Morris Bridgeman, Portland, secretary, Oregon State Medical Society; Mr. Clyde Foley, executive secretary, Oregon State Medical Society and secretary of the conference; Charles Manlove, hospital executive of Portland; Charles Hunt, Eugene, president-elect, Oregon State Medical Society; Karl Martzloff, Portland, member of the council of the Oregon State Medical Society. Other members of the Council of the Oregon State Medical Society were Leslie Kent, Eugene; Frank Power, Salem, and George Henton, Portland. Ralph A. Fenton, Portland, trustee of the American Medical Association, was also present. Washington was represented by Harry Rhodhamel, Spokane, president of the Washington State Medical Association; V. W. Spickard, Seattle, secretary of the Washington State Medical Association; Mr. Jack Geoffroy, executive secretary, Washington State Medical Association; Ray Zech, Seattle, delegate to the American Medical Association; C. W. Knudson, president, King County Medical Society and Washington Public Health League; H. D. Dudley, Seattle, director of the Medical Defense Fund, and H. L. Hartley, Seattle, assistant editor, *Northwest Medicine*. Idaho was represented by Frank Gibson, Potlatch, president, Idaho State Medical Association, and J. N. Davis, Twin Falls, secretary. The California delegation consisted of George Kress, San Francisco, secretary of the California Medical Association and editor of *California and Western Medicine*; George Reinle, Oakland, and Charles Dukes, Oakland.

## OFFICIAL NOTES

### WITNESSES BEFORE THE SPECIAL GRAND JURY IN WASHINGTON

The following witnesses are reported to have appeared before the Special Grand Jury in Washington: Dr. William W. Bauer, Chicago, director of the Bureau of Health Education, who presented the documents which had been subpoenaed from the American Medical Association headquarters; Mr. Theodore Wiprud, secretary of the Medical Society of the District of Columbia, who presented further documents to the jury, and Dr. Francis X. McGovern, chairman of the executive committee of the Medical Society of the District of Columbia.

### RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company, entitled "Your Health," began Wednesday October 19 and will run consecutively for thirty-six weeks. The program is broadcast each Wednesday over the Blue network of the National Broadcasting Company at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).<sup>1</sup>

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

December 28.	Good Milk. Good for You.
January 4.	Fool's Gold.
January 11.	Only a Cold!

### THE ST. LOUIS SESSION

#### Application for Space in the Scientific Exhibit Must Be Made by January 5

Attention is drawn to the fact that applications for space in the Scientific Exhibit at the St. Louis Session will close on January 5. Application blanks will be sent on request to the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago.

### CALIFORNIA APPROVES PLAN FOR MEDICAL CARE

At a special meeting of the house of delegates of the California Medical Association in Los Angeles December 17 a plan to provide medical care to residents of the state at a cost of about \$2.50 a month was approved. According to the *New York Times*, patients will select their own doctors and hospitals. Payments will be made on a weekly, monthly or semimonthly basis. Physicians will be paid on a unit basis, the payments graded from single units for minor services to twenty-five or more units for major operations. It is expected to take about six or eight months to put the plan into operation. While the exact cost has not been determined, the estimate is \$2.50 a month for each person. No provision for family group insurance was made under the revised final plan. Hospital, medical and surgical attention will be provided and the expense may be lower if 500,000 or more persons participate in the plan.

1. Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.

## Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ADDITIONAL MEDICAL COLLEGE NEWS AND ARTICLES APPEAR IN THE STUDENT SECTION, PAGE 2444.

### CALIFORNIA

**Changes in Health Officers.**—Dr. William A. Clarke has been appointed health officer of Holtville to succeed Dr. Harry B. Graeser. The city of San Mateo has contracted with the county of San Mateo to administer its public health under the county health unit, of which Dr. Charles C. Gans, Redwood City, is health officer. Dr. James A. Warburton has served for many years as health officer of the city.

**Annual Surgical Meeting.**—The Los Angeles Surgical Society held its annual meeting at the Los Angeles County General Hospital and the Los Angeles County Medical Association Building December 9-10. In addition to clinics the following papers were presented among others:

- Dr. John W. Budd Jr., Intraductal Papilloma and Carcinoma of the Breast.
- Dr. Rafe C. Chaffin, Surgical Drainage, Special Application of the Suction Principle.
- Dr. Alvin G. Foord, Physiologic Changes in the Leukocyte Count.
- Dr. Edward C. Pallette, Liver Abscess with Perforation.
- Dr. Harold L. Thompson, Mortality of Acute Perforation of Peptic Ulcer.
- Drs. George H. Houck and Frank S. Dolley, Amebiasis with Liver Abscess and Spontaneous Bronchial Drainage.

### CONNECTICUT

**Study of the Human Element in Motor Accidents.**—A comprehensive study of the human element in motor vehicle accidents will be made at the Institute of Human Relations of Yale University, New Haven, according to the *New York Times*. Cooperating will be the American Association of Motor Vehicle Administration, which instigated the project, and the Standard Oil Company of New Jersey, which is providing the funds. The association of motor vehicle administrators is composed of state officials who are directly concerned with the regulation of motor vehicles. The state motor vehicle commissioners will give the use of their departments so that research work can be carried on in various states. Complete reports will be made available to the project and the administrators will also furnish assistants to cooperate in individual studies. The association has also appointed a committee to cooperate in the project. The Standard Oil Company will make available its driver records and its safety and motor vehicle operating information.

### IDAHO

**Hospital News.**—A county hospital for Oneida County was recently dedicated at Malad.—PWA funds have been granted for a hospital in Lewis County at Nez Perce. The grant was \$8,100, and 55 per cent of the cost of the hospital will come from a bequest from Charles E. Burkhart.—A general hospital is to be built at Grangeville with a PWA grant of \$17,286 and \$22,000 collected and pledged by the city.

**Society News.**—Dr. Samuel M. Poindexter, Boise, discussed coronary disease before the Pocatello Medical Society in Pocatello November 23. At this meeting members of the former Upper Snake River Medical Society, including the territory from Rexburg to Ashton, asked for permission to withdraw from the Pocatello society in order to reorganize in their own territory.—Drs. Joseph Melvin Asprey and Norman R. Brown, Spokane, Wash., addressed the North Idaho Medical Society, Lewiston, October 19 on "Newer Developments in the Treatment of Cancer" and "Certain Problems of Treatment of Fractures" respectively. A film on "Typing of Pneumococci and Serum Treatment of Pneumonia" was shown.

### ILLINOIS

**Dedication of New Buildings at State Hospital.**—New buildings at Anna State Hospital, erected during the past five years at a cost of \$1,275,121, were dedicated October 15. Mr. A. L. Bowen, director of the state department of public welfare, gave the dedicatory address. The recreation hall in which the ceremonies took place was named in honor of the late Dr. Ralph A. Goodner; other buildings have been named

for Drs. W. C. Lence and William L. Athon, former managing officers of the institution. A portrait of Dr. Goodner was unveiled. Funds for remodeling and new buildings were supplied through state appropriation and PWA grants. The Athon and Lence cottages are of the one story "E-type" construction which is standard for state mental hospitals and contain 120 beds each. A 132 bed diagnostic center and hospital is now nearing completion.

### CHICAGO

**Society News.**—The Chicago Society of Internal Medicine was addressed December 19, among others, by Dr. Louis R. Limarzi and Emil M. Schleicher on "The Reaction of Peripheral Blood and Bone Marrow in Chronic Hemorrhage and in Essential Thrombocytopenic Purpura," and Dr. Carl C. Pfeiffer, "Effect of Analeptic Drugs in Hibernating Ground Squirrels."—Dr. Mabel E. Gardner, Cincinnati, addressed a joint meeting of the Chicago Council of Medical Women and the American Medical Women's Association November 9 on "Medical Women versus War."—At a meeting of the Chicago Roentgen Society November 10 Dr. Paul H. Holinger, among others, discussed "Biplane Fluoroscopy as an Adjunct to Bronchoscopy."—The Chicago Pediatric Society was addressed November 10 by Drs. Harold C. Stuart, Boston, and Mandel Sherman on "The Observation of Growth in Pediatric Practice: Useful Research Contributions" and "Classification and Interpretation of Neurotic and Abnormal Behavior of Children" respectively.—At a meeting of the Chicago Pathological Society November 14 Drs. George J. Rukstinat and Robert J. Hasterlik, among others, spoke on "Congenital Absence of the Penis."

### KANSAS

**Causes of Death in Kansas.**—There were 19,287 deaths recorded in Kansas during 1937. Of this total, 13,797 deaths, or 71 per cent, were the result of the ten leading causes, 7,924 in men and 5,873 in women, according to the *Medical Bulletin* of the Sedgwick County Medical Society. Heart disease continued to lead the causes of death with a total of 3,192 and following, in the order named, are the remainder comprising this group: cancer, accounting for 2,168; cerebral hemorrhage, 1,733; chronic nephritis, 1,590; "all accidents," 1,492; pneumonia, 1,126; diseases of the coronary arteries, 792; influenza (all forms), 686; motor vehicle accidents, 520, and tuberculosis, 498.

**Society News.**—Dr. Sumner L. S. Koch, Chicago, addressed the Shawnee County Medical Society in Topeka, October 3, on "Surgical Principles in Care of Injuries and Infections of the Hand."—At a meeting of the Bourbon County Medical Society in Fort Scott, October 24, Drs. Caryl R. Ferris and Claude J. Hunt, Kansas City, Mo., discussed "Advances Made in the Treatment of Diabetes" and "Problems in Thyroid Diseases," respectively.—The Marion County Medical Society was addressed in Marion October 25 together with the McPherson and Harvey county medical societies. Dr. Christian A. Hellwig, Wichita, spoke on "Analysis of Causes of Uterine Bleeding After the Age of 40 Years" and Philip W. Morgan, Emporia, "Electrocardiography and the Evaluation of Heart Symptoms."—Dr. Thomas L. Foster, Larned, discussed "New Treatments of Insanity" before the Pawnee County Medical Society in Larned recently.

### KENTUCKY

**District Meeting.**—The Sixth and Seventh Councilor Districts of the Kentucky State Medical Association held a joint meeting in Somerset November 4. The speakers included Drs. Harry S. Andrews, Louisville, "Management of Premature Infants"; Nevil M. Garrett, Brodhead, "Immediate Repair of Perineal Lacerations," and John W. Scott, Lexington, "Common Diseases of the Liver and Gallbladder."

### MARYLAND

**Expansion of Tuberculosis Activities.**—With funds made available by the Maryland Tuberculosis Association, Dr. Raymond Hussey, Baltimore, has been appointed field medical investigator for applicants for admission in state sanatoriums from Baltimore. Provision has been made also for two public health nurses. The board of managers of the state tuberculosis sanatorium commission has felt the need of an improved method of admitting patients. Heretofore applications have been sent directly to the superintendents of the various institutions and admissions were made in the order in which the applications were received. This has not proved

entirely satisfactory. Under the new plan Dr. Hussey will receive all applications from persons living in Baltimore and investigate each case with particular reference to the suitability of the patient for sanatorium care and the need for isolation. Dr. Hussey will visit the patient with or without the family physician and will take the necessary steps for admission without charge to the patient. Buildings now under construction for 200 additional patients will be ready for occupancy Oct. 1, 1939. In addition, the board of managers plans to request the next legislature for funds to provide for an extra 100 beds at Henryton, the sanatorium for colored persons, and to establish a branch hospital for colored patients on the Eastern shore.

### MASSACHUSETTS

**Departments of Tropical Medicine and Comparative Pathology Merged.**—The department of tropical medicine, Harvard University Medical School, Boston, and the department of comparative pathology have been consolidated. The change was effected on the retirement of Dr. Richard P. Strong early this fall as professor of tropical medicine. The combined department is now under the supervision of Dr. Ernest E. Tyzzer, George Fabyan professor of comparative pathology.

**Society News.**—At a meeting of the Boston Society of Psychiatry and Neurology October 20 the speakers were Drs. Arthur L. Watkins on "The Cerebrospinal Fluid in Retrobulbar Neuritis" and Michael S. Burman, New York, "Observations on Spastic Paralysis and Dystonia Musculorum Deformans."—Dr. William H. Watters, Boston, addressed the New England Society of Physical Medicine October 19 on "Physical Medicine in Chronic Disease."—At a meeting of the Harvard Medical Society in Boston October 25 Dr. Henry A. Christian, Boston, spoke on "Certain Cardio-renal Circulatory Correlations."—Dr. George E. Hall, Toronto, discussed "Neurogenic Influences in Experimental Coronary Artery Disease" before the New England Heart Association in Boston October 26.

**Director of New Department of Mental Health.**—Dr. Clifton T. Perkins, acting commissioner, state department of mental diseases, has been appointed commissioner of the new state department of mental health and Dr. Bardwell H. Flower, assistant superintendent of the Grafton State Hospital, was appointed assistant commissioner. The department is the outgrowth of a recent reorganization of the state department of mental diseases, of which Dr. David L. Williams was the former commissioner. The law authorizing the change was enacted July 7. Dr. Perkins graduated at the Boston University School of Medicine in 1926. Subsequently he served on the staff of the Worcester State Hospital, as assistant to the commissioner of mental diseases, assistant commissioner and acting commissioner, and as a member of the faculty in the department of psychiatry in his alma mater.

### MICHIGAN

**Society News.**—Dr. Leo G. Rigler, Minneapolis, addressed the Calhoun County Medical Society in Battle Creek November 1 on "X-Ray Diagnosis of Acute Abdominal Conditions."—A symposium on the serum treatment of pneumonia was presented before the Washtenaw County Medical Society, Ann Arbor, November 8, by Drs. Abbott B. Mitchell, Lansing, Cyrus C. Sturgis, Herman H. Riecker and Dorman E. Lichty, Ann Arbor.—Dr. Frank A. Kelly, Detroit, discussed "Injection Treatment of Hernia" before the Genesee County Medical Society in Flint November 2. Dr. Douglas Donald, Detroit, discussed "Pitfalls in Diagnosis of Coronary Thrombosis" before this society in Flint November 16.—Dr. Frederick H. Falls, Chicago, addressed the Kalamazoo Academy of Medicine November 15 on "Early Recognition and Treatment of Cancer of the Cervix and Uterus."

**Home for Convalescent Girls.**—A home for convalescent girls in Detroit, the first in the state, has been established by Dr. B. Raymond Hoobler, emeritus professor of pediatrics, Wayne University College of Medicine, as a memorial to his wife, the late Madge Sibley Hoobler. Organized as a non-profit corporation, the Hoobler Guest House, with accommodations for twenty-five persons, was dedicated November 27. If the girl is under the care of a physician, she obtains his permission to go to the guest house. All admissions are made through Alice M. Walker, head of social service at Harper Hospital. When admitted, a girl may spend as much as two weeks without cost in an atmosphere of quiet refinement and healthful living. The guest house is the outcome

of a wish expressed by the late Mrs. Hoobler, who intended to dedicate it to her mother. According to the *Detroit Free Press*, Dr. Hoobler plans to make the present house the first of several in Detroit.

### MINNESOTA

**Program of Health Education.**—A coordinated program of health education, working through a committee representing interested agencies, is under way in Minnesota. A special topic will be chosen each month for discussion by hospital staffs and local societies, while the state medical society and the state board of health will send out bulletin information. The motion pictures, radio and weekly news services of the state society and other public health agencies will be utilized in disseminating information to the public. A tentative list of topics has been announced: January, pneumonia; February, pediatrics; March, degenerative and circulatory diseases; April, cancer; May, obstetrics and gynecology; September, traumatic surgery; October, syphilis and gonorrhea; November, tuberculosis and respiratory diseases, and December, anemias and deficiency diseases.

### MISSOURI

**Hospital News.**—Construction on a new state trachoma hospital on a three acre site adjoining the city of Rolla started November 29. Citizens of Rolla donated the property, and the \$75,000 appropriated by the state legislature will be supplemented by a federal grant of \$63,000.

**Society News.**—The Jackson County Medical Society has revised its charter and by-laws, effective January 1. The first election to be held under the new laws, however, will be held in 1940.—The Wyandotte County Medical Society was addressed in Kansas City November 15 by Dr. William Walter Wasson, Denver, on "The Anatomy, Physiology and Mechanics of the Chest as the Basis for Study and Classification of Diseases of the Chest."

### NEBRASKA

**District Meetings.**—At the annual meeting of the Seventh Councilor District Medical Society in Superior October 20 the speakers were Drs. Robert J. Stearns, Omaha, diseases of the cervix, exclusive of those secondary to birth injuries; Harold S. Morgan, Lincoln, "Etiology and Symptomatology of Injuries of the Birth Canal Due to Birth Injuries," and Maurice E. Grier, "Treatment of Injuries of the Birth Canal Due to Birth Injuries."—The Sixth Councilor District of the Nebraska State Medical Association met in Wahoo November 14 with the following speakers: Drs. Arthur L. Miller, Kimball, president-elect of the state association, on "Medicine of Tomorrow"; Herman F. Johnson, Omaha, "Treatment of Fractures of the Upper Extremities," and James E. M. Thomson, Lincoln, who presented a motion picture on "Fractures of the Spine."

### NEW JERSEY

**Personal.**—Dr. Earl S. Hallinger, Camden, was elected secretary of the State Board of Medical Examiners November 16 to succeed the late Dr. James J. McGuire.

**Thirty-Four Aliens Pass State Examinations.**—Thirty-four physicians who are refugees from various European countries passed a recent examination for licenses to practice in New Jersey, it is reported. They received six year licenses, which will continue in force if they become citizens within the period; otherwise the licenses will be automatically annulled. Twelve refugee candidates failed, according to the report. Forty-five of a class of fifty-eight citizens passed the examination.

**Society News.**—Dr. William Seaman Bainbridge, New York, addressed the Camden County Medical Society, Camden, December 6 on "The Cancer Problem of Today," with Dr. William Wayne Babcock, Philadelphia, as commentator.—Dr. Oswald S. Lowsley, New York, addressed the Academy of Medicine of Northern New Jersey, Newark, December 15, on "Some New Operative Procedures in Urology."—Col. Jay W. Grissinger, surgeon, Second Corps Area, U. S. Army, and Capt. Charles M. Oman, senior medical officer, Third Naval District, U. S. Navy, addressed the Essex County Medical Society, Newark, December 8, on "The Medical Profession in Relation to Military Preparedness."—Drs. John B. Flick, Philadelphia, and Berthold S. Pollak, Secaucus, addressed the Atlantic County Medical Society, Atlantic City, December 9, on surgical and medical treatment, respectively, of pulmonary tuberculosis.—Dr. Byron P. Stookey, New

York, addressed the Bergen County Medical Society, Hackensack December 13 on "Recent Developments in the Diagnosis and Treatment of Low Back Pains and Sciatica with Special Reference to Herniations of the Nucleus Pulposus."—Dr. Harvey F. Doe, Montclair, discussed the state program on pneumonia at a meeting of the Hudson County Medical Society, Jersey City, November 1. A film on serum treatment was shown.

## NEW YORK

**Obstetric Institute in Syracuse.**—An obstetric institute sponsored by the maternal welfare committee of the Onondaga County Medical Society was presented at the Syracuse University College of Medicine December 8. Among the subjects discussed were the use of sulfanilamide, use and interpretation of the Friedman test, home delivery technic, anesthesia and danger signals during labor. At a luncheon meeting Dr. Herman G. Weiskotten, dean of the medical school, spoke on opportunities for graduate studies in obstetrics.

## New York City

**Examinations for Physicians.**—The Municipal Civil Service Commission announces an examination to be held for physicians in the department of correction. There are four vacancies for women in the House of Detention and six for men at Rikers Island. The salary ranges from \$1,360 to \$1,800 a year. Full time service is required, with maintenance in certain cases. Candidates must be graduates of reputable medical schools and must have one year's experience as intern in a hospital of recognized standing or equivalent medical experience. They must be licensed to practice in New York before certification. Applications will be received up to Wednesday December 28.

**Medical Equipment for World's Fair.**—An automobile x-ray unit has been built for the medical division of the New York World's Fair. With the mobile unit the eight first aid stations will be provided with immediate x-ray service, especially in cases of suspected fractures or other internal injuries. Plates will be developed in the darkroom in the automobile, which is equipped with a dry ice device to keep the developer chemicals at the maximum level of efficiency. A special ambulance is being prepared for the work of the "division of pneumatology," which will have charge of administering gases at first aid stations and at two resuscitation centers. The ambulance will be fitted with modern equipment for care of all kinds of asphyxial accidents, such as asphyxiation from gas, submersion and fire fighting.

**Society News.**—Dr. Malcolm Goodridge was elected president of the New York Academy of Medicine for a two year term, succeeding Dr. James Alexander Miller. Dr. Rufus I. Cole, Mount Kisco, was elected vice president for three years and Dr. Bernard Sachs was made treasurer for three years.—The Physicians' Square Club of Greater New York held its one hundred and fiftieth dinner December 14 at the Hotel Westover. Dr. A. Bern Hirsh, editor of *New York Medical Week*, was the guest speaker on "Fifty Years in Medicine and Masonry."—A symposium on endocrinology was presented at the first fall meeting of the International Spanish Speaking Association of Physicians November 30 by Drs. James R. Goodall, Montreal, Canada; William F. Rienhoff Jr., Baltimore, and Murray B. Gordon, New York.

**Gifts to Columbia.**—Columbia University has received \$403,792.59 in cash gifts for medical purposes within recent months. Among the most important are the following:

Rockefeller Foundation, \$111,750; of this \$100,000 is to be for research in neurology over a five year period, \$7,000 for research on constitutional aspects of disease, \$2,750 for studies on the common cold and \$2,000 for research in chemical embryology.

Carnegie Corporation of New York, \$64,460; of this \$50,000 is for endowment of the program for graduate medicine, \$8,260 for chemical research in the department of biologic chemistry and \$1,500 for research on deficiency diseases in certain animals.

John and Mary R. Markle Foundation, \$54,800; of this \$24,600 is for cancer research at the Institute of Cancer Research on biologic effects of radiation.

Josiah Macy Jr. Foundation, \$26,260 for various departments. An anonymous donor, \$20,000 for research at the Institute of Cancer Research.

William J. Matheson Foundation, \$2,400 for the Matheson Encephalitis Fund in the department of bacteriology.

Philip Morris and Company, \$2,000 for research in pharmacology.

**Hospital Council Formed.**—The Hospital Council of Greater New York was formed at a meeting of various agencies November 10. It supersedes the Hospital Council of the City of New York formed in 1935, according to the *New York Times*. The council will be composed of seventeen organizations. They include the Coordinating Council of the Five County Medical Societies of New York City, New York

Academy of Medicine, United Hospital Fund, Merchants Association of New York and New York Board of Trade besides welfare, civic and religious groups and the city of New York. Its aim is to "improve and coordinate the services of hospitals and related health agencies" and to "plan the economical and efficient development of these services in relation to community needs." A planning committee of twenty-nine members will be in charge of the council's program.

## OHIO

**Postgraduate Day in Akron.**—Three Cincinnati physicians provided the program of the Summit County Medical Society's seventh annual Postgraduate Day November 16. Dr. Max M. Zininger spoke on "Surgical Lesions of the Stomach and Duodenum" and "Diagnosis and Surgical Treatment of Diseases of the Gallbladder and Bile Ducts"; Dr. Marion A. Blankenhorn, "Serum Treatment of Lobar Pneumonia" and "Bacterial Endocarditis"; John A. Caldwell, "Fractures of the Humerus" and "Fetish Worship in the Treatment of Fractures."

**District Meeting.**—The Ninth Council District of the Ohio State Medical Association held a meeting in Ironton November 16. Dr. Parke G. Smith, Cincinnati, president-elect of the state association, spoke on economic problems of the profession and Mr. Charles S. Nelson, Columbus, executive secretary, on organization matters. The scientific program was as follows: Drs. George W. Crile, Cleveland, on "Surgical Treatment of Hypertension"; Julian E. Benjamin, Cincinnati, "Functional Heart Tests," and Jonathan Forman, Columbus, "Allergy in Everyday Practice."

## OKLAHOMA

**Society News.**—At a meeting of the Carter County Medical Society in Ardmore October 17 the speakers were Drs. Leonard S. Willour, McAlester, on fractures; Glenn J. Collins, McAlester, the electrocardiograph as an aid in diagnosis, and Lyman C. Veazey, Ardmore, psychiatry in medicine.—Drs. Henry H. Turner and William M. Taylor, Oklahoma City, addressed a joint meeting of the Grady, Stephens and Caddo county medical societies recently at Anadarko on "Practical Endocrinology" and "Acute Respiratory Diseases of Childhood" respectively.—Drs. Carroll M. Pounders and George H. Garrison, Oklahoma City, addressed the Garfield County Medical Society, Enid, November 30, on "Juvenile Rheumatism" and "The Present Status of Poliomyelitis—Its Early Diagnosis and Treatment" respectively.

## OREGON

**Pacific Coast Medical Conference.**—The Oregon State Medical Society was host December 4 to a conference of state medical societies of the Far West in Portland. The Idaho, Nevada, Arizona, California and Washington associations were invited. Among topics discussed were methods of publicizing organization activities and policies, medical care of low wage groups, Farm Security Administration plans for medical care, industrial commission contracts with hospital associations and other corporations, the American Medical Association survey, graduate instruction, malpractice insurance, cooperation with other groups, legislative organization and technic.

## PENNSYLVANIA

**Graduate Assembly in Danville.**—The first graduate assembly of the year under the auspices of the Montour County Medical Society was held at Geisinger Hospital, Danville, November 18. The guests were Drs. Eugene F. Du Bois, New York, who spoke on "Temperature Regulation and Fever"; Charles C. Higgins, Cleveland, on "Renal Calculi—Etiology, Diagnosis and Treatment," and James H. Means, Boston, who conducted a clinic on heart disease. Dr. David W. Thomas, Lock Haven, president of the Medical Society of the State of Pennsylvania, spoke at a luncheon on "Postgraduate Seminars in Pennsylvania."

## Philadelphia

**Alumni Seminar for Pharmacists.**—The Philadelphia College of Pharmacy and Science has announced plans for a three day seminar for practicing pharmacists to give them a review of the latest developments in pharmacy, chemistry, bacteriology and biology. The dates are January 30 to February 1 during the midterm recess of the college. Subjects on the program for the lectures and demonstrations include dispensing of the new chemotherapeutic agents; demonstrations in physicochemical methods; endocrines, vitamins and hormones; the newer biologicals, and where to go for information on scientific prob-



lems. Any pharmacist, graduate of a recognized college of pharmacy, is eligible for enrolment. Full information may be obtained from John E. Kramer, B.Sc., registrar, Philadelphia College of Pharmacy and Science.

**Society News.**—Dr. Philip D. McMaster, New York, addressed the Pathological Society of Philadelphia November 10 on "Skin Lymphatic and Lymph Flow in Health and Disease" and Dr. Stanley P. Reimann and Mr. Barnard J. Miller, on "The Parthenogenic Extrusion of Polar Bodies from an Unfertilized Human Ovum."—At a meeting of the Northern Medical Association of Philadelphia November 21 the speakers were Drs. Leslie N. Gay, Baltimore, on "Complications of Bronchial Asthma and Their Treatment"; Aaron Brown, New York, "Pollen Desensitization and Its Complications," and Matthew S. Ersner, "Indications and Contraindications of Rhinologic Regimen and Surgical Intervention in Bronchial Asthma."—Dr. Edgar G. Ballenger, Atlanta, Ga., addressed the Philadelphia Urological Society November 28 on "Persistent Gonococcal and Other Infections."—Drs. Charles Mazer and George Baer, among others, addressed the Obstetrical Society of Philadelphia December 1 on "Therapeutic Value of Low-Dosage Irradiation of the Pituitary Gland and Ovaries in Functional Menstrual Disorders and Sterility."

### SOUTH CAROLINA

**Society News.**—South Carolina members of the South Atlantic Association of Obstetricians and Gynecologists held a meeting in Columbia November 5 with the committee on maternal welfare of the South Carolina Medical Association. Dr. Joseph Decherd Guess, Greenville, made an address on "The Problem of the Occiput Posterior Position" and Dr. John M. Fleming, Spartanburg, presented a paper on "Endometriosis of the Round Ligament." Motion pictures dealing with the investigation of sterility and with vaginal hysterectomy were shown.—Dr. Foster M. Routh, Columbia, addressed the Ridge Medical Society in Batesburg recently on allergy.—Dr. George H. Bunch, Columbia, discussed appendicitis at a meeting of the Coastal Medical Society in Walterboro October 27.

### TEXAS

**Society News.**—Dr. Charles T. Stone, Galveston, addressed the Bexar County Medical Society, San Antonio, October 6 on "The Physiologic Basis for the Treatment of Peptic Ulcer."—Drs. Sidney J. Wilson and Truman C. Terrell, Fort Worth, addressed the Tarrant County Medical Society, Fort Worth, October 4, on "Treatment of Mycosis Fungoides" and "A Comparative Study of Foille with Tannic Acid and Tannic Acid Preparations in the Treatment of Burns" respectively.—Drs. Carl Kaufman and Sam V. Granata, Beaumont, addressed the Jasper-Newton Counties Medical Society, Kirbyville, November 16, on asthma and allergy.—A symposium on fractures was presented before the Dallas County Medical Society November 10 by Drs. Charles F. Clayton, Fort Worth; James S. Speed, Memphis, Tenn., and Charles S. Venable, San Antonio.

### WEST VIRGINIA

**State Health Conference.**—Dr. Edwin Cameron, Morgantown, was elected president of the West Virginia Public Health Association at the annual conference in Bluefield October 31-November 2. Drs. Bruce H. Pollock, New Cumberland, and Claude A. Thomas, Martinsburg, were elected vice presidents. Among the speakers were Miss Katherine Lenroot, chief of the Children's Bureau, Washington, D. C.; Dr. Goldsborough Foard McGinnes, director of the bureau of communicable diseases, state department of health of Virginia, Richmond, and Dr. Mark V. Ziegler of the U. S. Public Health Service, Washington, D. C.

### WISCONSIN

**Dr. Sleyster Guest of Honor.**—The Medical Society of Milwaukee County and the Woman's Auxiliary held their annual dinner meeting December 8 at the Milwaukee Athletic Club with Dr. Rock Sleyster, Wauwatosa, President-Elect of the American Medical Association, guest of honor. Dr. Ernest E. Irons, clinical professor of medicine, Rush Medical College, Chicago, was the guest speaker and his subject "The Last Illness of Sir Joshua Reynolds."

**State Tuberculosis Meeting.**—The thirtieth annual meeting of the Wisconsin Antituberculosis Association was held in Milwaukee October 27-29. Dr. Frank J. Hirschboeck, Duluth, Minn., was the principal speaker at a medical meeting and clinic Thursday evening. The annual dinner was held Friday evening with Dr. Rock Sleyster, Wauwatosa, President-Elect

of the American Medical Association, as toastmaster. At a health education meeting Saturday the speakers were Dr. Paul A. Teschner, Chicago, assistant director, Bureau of Health Education, American Medical Association, on "Who Shall Teach?" and Dr. Amelia T. Wood, Muncie, Ind., "What Shall Be Taught?"

### GENERAL

**Social Hygiene Day.**—February 1 has been named as the date for the third observance of National Social Hygiene Day. An anonymous gift of \$15,000 for the \$500,000 fund sought by the National Anti-Syphilis Committee of the American Social Hygiene Association was recently announced. This brings the fund to \$187,065. The association has formulated an eight point program including plans to organize more local and state committees to fight gonorrhea and syphilis, encourage passage of laws for prevention of syphilis, fight prostitution and medical quackery, aid employers and employees against the economic losses caused by these diseases, extend information on social hygiene to the youth of America, expand the personal advisory and consultation service, guide parents, teachers and pastors in sound principles of sex education of youth, and continue observations and reports to citizens regarding official programs. "Guard Against Syphilis" has been chosen as the slogan for the 1939 observance of National Social Hygiene Day.

**New Prize for Vitamin Research.**—To promote interest in research on the water-soluble "B-complex" vitamins, Mead Johnson and Company, Evansville, Ind., has established an annual award of \$1,000 to be presented over a period of five years through the American Institute of Nutrition. A committee of members of the institute will select the recipient, and the presentation will be made a feature of its annual meeting each spring. The award will be given to the laboratory (nonclinical) or clinical research worker in the United States or Canada who in the opinion of the judges has published during the previous calendar year the most meritorious report dealing with the B-complex vitamins. If circumstances and justice dictate, the prize may be divided among two or more persons or it may be given to a worker for valuable contributions over an extended period, but not necessarily representative of a given year. Nominations may be sent at any time to Leonard A. Maynard, Ph.D., Laboratory of Animal Nutrition, Cornell University, Ithaca, N. Y. To be considered for the award at any given spring meeting, the nomination must be received by January 15.

**Medical Activities of the Red Cross.**—Important features of the activities of the American Red Cross during the past year, according to the annual report, were pellagra control, volunteer blood donor service, oral hygiene and venereal disease control. Red Cross public health nurses made 1,043,954 field visits, 214,398 of them on behalf of mothers and infants, during the fiscal year ended June 30. Each year the number of certificates issued for courses in home hygiene and care of the sick increases; the total number since the first awards in 1914 is 951,639. To prepare teachers for these courses, ninety-five institutes were held last year; nine colleges now give summer teacher training courses for this work. At the end of the third year of the highway emergency first aid program 2,454 stations had been established. Rigid inspection of these stations is maintained, the report says, and those not meeting the standards are withdrawn. Seventy-two agreements have been made with cooperating organizations designating 2,051 pieces of highway equipment as mobile first aid units. This was also the third year of the program of home and farm accident prevention. This activity has become an integral part of the Junior Red Cross program and has stimulated concern about accidents in school environments as well. Expenditures for the fiscal year amounted to \$10,358,566.21 and the resources as of July 1 to \$14,514,902.38. The year was marked by the death of Admiral Cary T. Grayson, the chairman, and appointment of Mr. Norman H. Davis to succeed him.

### CORRECTION

**Pathology of Rheumatoid Arthritis.**—In the abstracts of the meeting of the American Rheumatism Association, in the discussion given by Dr. D. Murray Angevine on page 2042 of the November 26 issue, the sentence reading "I trust that we have not given the impression that we feel certain that there is an atypical pathologic picture for rheumatoid arthritis" should have been "I trust that we have not given the impression that we feel certain that there is a typical pathologic picture for rheumatoid arthritis."

## Foreign Letters

### LONDON

(From Our Regular Correspondent)

Nov. 26, 1938.

#### Medicine and Penal Reform

The criminal justice bill, which has been introduced in the House of Commons by the government, marks a big advance in dealing with young offenders. Institutions to be called "remand centers" are to be provided, to which such offenders when remanded or committed for trial in custody are to be sent instead of to prison. There will also be "remand homes" for problem children and persons under 17 who require medical observation. Offenders between 16 and 21 whose offenses justify a period of Borstal training are to go to institutions called Howard homes, which will exercise a system of residential control, but they will be able to go out to their ordinary employment. There will also be public hostels for young persons who ought to be sent away for a time from their homes or from places where they have fallen into bad associations. Another interesting experiment is the establishment of "compulsory attendance centers," where young persons sentenced for minor offenses may be sent and avoid imprisonment. They will be required to attend during half holidays or in the evening after work.

Another most important reform is abolition of the power of the courts to pass sentences of corporal punishment, which is reserved for serious prison offenses. Others are two new types of prison sentences, corrective training and preventive detention. The former will be for not less than two or more than four years for persons between 21 and 30 whose records make such sentences expedient. Preventive detention is for persons over 30 whose records make this necessary for the protection of the public. Such sentences may range from four to ten years. The Broadmoor institution for criminal lunatics is to be transferred to the management of the board of control, the body which controls the administration of mental hospitals.

This bill, which is the latest development of the modern tendency to make the criminal law more humane by helping to reform instead of simply punishing the offender, does not touch the vexed question of criminal responsibility. The tendency of psychiatrists to regard crime as a form of mental disease is by no means shared by judges and lawyers. At a meeting of the Hunterian Society, the psychiatrist Dr. Henry Yellowlees opened a discussion on the thesis that the psychologic treatment of the criminal is preferable to the punishment of the crime. He said that our penal system was becoming less vindictive, more reformatory and more humane. Society was beginning to recognize its duty to the criminal. The highest expression of that duty lay in regarding him as a mentally sick man. Many an antisocial act was committed under the pressure of an irresistible psychologic force, all the more terrible in that it was not consciously realized. But psychotherapy could not be applied to the whole criminal picture indiscriminately. Some criminals it could not help; it was a failure in the absence of sincere, willing and persistent cooperation of the patient. It was the duty of the law to decide what criminals would respond to the appeal of psychotherapy, but its criteria of criminal responsibility in cases of glaring insanity showed how unqualified it was to decide the matter.

In the discussion, lawyers took part. While they admitted that it would be better for many prisoners to be treated psychologically, that did not mean that they should be sent to a hospital and not to prison. The fear of prison was a valuable deterrent. One claimed that Dr. Yellowlees had killed his own motion. Psychology, he said, had been described as a

science in its infancy, but it was in a prenatal stage, with little prospect of live birth. It had created a terminology and called it a science. The motion was carried by a large majority.

#### THE SOCIAL RELATIONS OF SCIENCE

The formation of an organization to study the social relations of science is proposed in the periodical *Nature*. Forty scientists, including Sir William Bragg (president of the Royal Society), Sir John Russell (director of the Rothamsted Agricultural Station), Sir F. Gowland Hopkins (professor of biochemistry, Cambridge), Prof. J. B. S. Haldane, Julian Huxley, H. G. Wells, and representatives of sociology, economics and psychology, comment on the need to go deeper into the repercussions which science has had on social development. From the platform of the British Association for the Advancement of Science, speakers have repeatedly urged the need for a scientific survey of the problems which confront civilization, problems largely the result of the discoveries of scientific workers. The American Association for the Advancement of Science officially expressed concern that "science and its applications are not only transforming the physical and mental environment of men but are adding greatly to the complexities of the social, economic and political relations among them." One of its representatives is coming over to discuss with the British association the problem of joint action. The International Council of Scientific Unions set up last year a committee to survey the influence of science on the world picture as well as on the material side of human life and society.

Julian Huxley asks "What research is being done in Great Britain, under what conditions and how financed? Why are some branches relatively neglected? What are the trends of research and its practical and social effects?" He visualizes an organization which would supply authoritative information. A code of ethics for scientific men is envisaged by Prof. A. V. Hill, secretary of the Royal Society. Secrecy in research, the patenting of discoveries of public value, advertisement, expert evidence, the exploiting of dangerous knowledge or the selling of dangerous drugs could form the subject matter of such a code.

### PARIS

(From Our Regular Correspondent)

Nov. 26, 1938.

#### Routine Preoperative Roentgenograms of the Chest

X-ray examination of the chest is employed as a routine in France in the examination of army and navy recruits, medical students, pupil nurses and applicants for government and private employment. This method of examination is simple and should be used in the evaluation of the risk of operative procedures in all hospital services. Professor Sergent of Paris has called attention to the danger of operation when there is pulmonary tuberculosis, and Bezançon and Jacquelin have studied the effect of operations in lighting up latent tuberculous foci in the lungs. A team composed of Professor Gosset, surgeon, Professor Etienne Bernard, phthisiologist, and Professor Ledoux-Lebard, radiologist, decided to examine all patients preoperatively, and the results of eleven instructive observations were submitted at the October 4 meeting of the Académie de médecine. Four of the operations were performed as emergencies and preoperative x-ray examination of the chest was not carried out. The later appearance of fever, cough and expectoration led to such examination after operation. In all four cases there were found advanced tuberculous lesions which had shown evidence of exacerbation after the anesthesia. In five cases preoperative x-ray examination revealed pathologic changes in one or both lungs. In one of these the presence of infiltration at one apex led to postponement of the operation until the pulmonary lesions had

improved. Operation was performed in one with local anesthesia and in one with spinal anesthesia without any ill effects, but in a third, in which general anesthesia was used, there was a marked rise in the temperature after operation and smears of expectorated material showed tubercle bacilli. In the tenth case there was some doubt before operation as to the existence of a pulmonary focus and general anesthesia was employed; it was followed by a marked exacerbation of a latent tuberculous lesion. In the eleventh case the preoperative x-ray examination failed to reveal any pulmonary focus but after operation the presence of a high temperature led to x-ray examination and bacteriologic examination of the sputum, which revealed an infiltration of the base of the right lung and the presence of tubercle bacilli.

The authors said that all patients should be subjected to x-ray examination of the chest as a routine part of the preoperative examination. If a definite focus is found, it is advisable to employ either local or spinal anesthesia or any general anesthetic other than ether. These precautions hold true for emergency operations.

In the discussion Professor Sergent emphasized that, although there are tuberculous foci which are not detected by the ordinary methods of physical diagnosis, there exist lesions which escape detection by x-ray examination. Hence both methods should be employed.

Professor Laubry said that he would enlarge the field of preoperative x-ray examination to include an examination of the heart and large vessels.

#### Action of Sulfanilamide-Pyridine on the Pneumococcus

The many advantages of sulfanilamide-pyridine over the older sulfanilamide was the subject of a paper by Dr. Raymond Benda read at the October 21 meeting of the Société médicale des hôpitaux of Paris. Dr. Benda stated that the newer preparation is far less toxic and that in 151 cases no cyanosis of the lips or nails had been noted. The only ill effects were anorexia, nausea and headache in one case. Dr. Benda reported five cases of pneumococcal infection in which sulfanilamide-pyridine had been given. The temperature of a patient aged 74 with a large area of consolidation became normal and the physical evidence of pulmonary involvement disappeared within forty-eight hours after the administration of 3 Gm. of sulfanilamide-pyridine. In another case both this drug and sulfanilamide had been given at intervals of several weeks, so that their action could be compared. The patient was a man 44 years of age suffering from a pulmonary abscess of pneumococcal origin. During the fourth week a daily dose of 3 Gm. of sulfanilamide had been given for five days without any improvement in the patient's condition. Dr. Benda saw him for the first time twelve days later and advised administration of 3 Gm. of sulfanilamide-pyridine. This was followed by a sharp drop in the temperature, which persisted for five days, but it was necessary to discontinue administration of the drug because of persistent nausea. The temperature rose again and remained up until the sulfanilamide-pyridine was given again twenty days later. After a second drop in the temperature to normal, the general condition improved to such an extent that operative intervention could be undertaken.

#### Streptococcal Empyema Cured by Sulfanilamide

At the same meeting three French naval surgeons, Drs. Germain, le Gallou and Morvan, reported a case of pleurisy on the right side involving the mediastinal aspect of the pleura and complicated by empyema due to the hemolytic streptococcus. Cure without operative intervention followed the use of sulfanilamide by mouth and intramuscular injection combined with evacuation of the pus by repeated punctures and injection of the drug into the pleural cavity.

## BERLIN

(From Our Regular Correspondent)

Nov. 15, 1933.

### Congress of the European Society of Mental Hygiene

The Congress of the European Society of Mental Hygiene was held at Munich late in August under the auspices of the German Committee for Mental Hygiene, a branch of the Society of German Neurologists. Professor Rüdin of Munich presided. The mental hygiene movement is recognized to have originated in America, to have slowly gained headway in other countries after 1905 and to have spread much more rapidly since the World War. The German Association for Mental Hygiene was founded in 1925; it was superseded in 1935 by the mentioned committee. In recent years the latter has stressed the problems of eugenics in conformity with the German national attitude.

Even at this congress of the European organization the first theme of discussion was "The Eugenic Marriage," introduced by Morgenthaler of Berne and Chairman Rüdin. Morgenthaler spoke on the selection of the marriage partner. In his opinion, every healthy person should marry. Conversely, he opposes the marriage of a person who may be classed as incurably a member of one of the following groups: the feeble-minded, the insane, excessively egocentric psychopaths, degenerate hysterics, drug addicts, homosexuals and manifest schizoids. He also is against the marriage of persons unsuited for a tranquil married life because of abnormal aggressiveness, passivity or introversion. More attention should be paid to those persons who, although basically fit for marriage, remain single because of timidity and similar psychic factors. The ministrations of a well regulated matrimonial agency should be of optimal service to this group. The youth should be definitely trained for marriage, and individual advice is desirable.

Rüdin lectured from the standpoint of the eugenic condition and hereditary endowment of the population as a whole. He pointed out that it is the first duty of a family physician who is schooled in eugenics to try to prevent all genetically and nationally undesirable mesalliances. In addition, social intercourse among boys and girls of families presenting hereditary defects and poor hereditary endowment should be deliberately discouraged. The theory that degenerate families can be "regenerated" by union with eugenically healthier persons is today looked on as unmoral and obsolete. It is difficult to make decisions with regard to persons who, although themselves free of hereditary defects, are possessed of tainted kindred. Here one is confronted with one of the most burning questions of genetic research, the heterozygote problem. Diagnostic possibilities as well as statistical data fail here.

In the discussion the importance of eugenics propaganda was ardently championed by two Italians, whereas Repond, a Swiss, urged that decisions with regard to marriage should be made with caution, since the civilized nations of the West have yet to hit on a generally acceptable "formula of marriage." Former Hamburg psychiatrist Weygandt, on the other hand, voiced the opinion that objectives such as the improvement and purification of hereditary characters cannot be attained without the use of force.

At the second session the problem of "Prophylaxis of Drug Addiction" was taken up. Stanojewitsch of Belgrade stated that addiction to narcotics is not an important problem in Yugoslavia. Russian immigrants are largely responsible for an increase in alcoholism as well as morphinism and cocaineism since the World War. Drunkenness is extremely rare among the country's Jewish population. Pohlisch of Bonn discussed the results of modern genetic and constitutional research studies of addicts. He disparaged the "Jewish psychology systems" of Freud and Adler, which attempt to place the responsibility

for the production of addiction on environmentally conditioned injuries to the psyche. He also accused these schools of working mischief by an arbitrary use of the terms "rausch" and "sucht," which tends to obscure and confuse heterogenic concepts. Conversely, research of recent years, based on natural scientific methods, has elicited proof that the circumstances and essential etiologic factors in cases of addiction should be looked for in the domain of endogenic, congenital, psychosomatic hereditary defects. The abnormal familial background of addicts is a matter of voluminous, statistical record of grave congenital defects. Numerous other factors ought not of course to be ignored. Also of interest are the racial-biologic differences which underlie the predilection of various peoples for particular addictions. Because of drastic legal restriction, addiction to opiates has become rather unimportant in Germany. The misuse of hypnotic drugs, on the contrary, should be a serious consideration of the medical profession.

In conclusion Panse spoke on hygienic and legislative measures against drug addiction, and Crime Commissioner Thomas, director of the National Antinarcotic Police Center, described various international measures in this field.

In the general discussion, mention was made of the great decrease in alcoholism in Italy. Fahreddin Kerim Gökey of Istanbul told of the Turkish government's campaign against addiction to drugs. This campaign is all the more noteworthy because these alkaloids represent a source of government income which should not be underestimated. In southern and western Anatolia hasheesh is the usual drug; in Istanbul it is heroin. Morphine and cocaine play minor parts.

Other reports dealt with child psychiatry and child psychology and the importance of occupational therapy in the treatment of mental and bodily illness.

#### The Purge of Jewish Physicians

Supplementary data can now be added to the recent reports on the purge of Jewish physicians (*THE JOURNAL*, September 17, p. 1118, and October 29, p. 1674). September 24 Professor Dr. Klare, "commissioner of the specialized medical press," issued the following statement: "In view of the fact that the German medical profession is now freed of all members of an alien race, the writings of Jewish authors ought not to appear in our German medical journals. At the same time I trust that our German doctors will subscribe only to those foreign journals which are published by Aryan organizations and edited by Aryan physicians. In this connection I should like to call attention to the emigration of the journal *Ars Medici*, together with its Jewish editor and publisher, Dr. Max Ostermann, from Vienna to Switzerland. From its new home this publication continues to solicit the subscriptions of German doctors, but I feel sure that our men will refuse to have anything to do with the Jewish publisher of *Ars Medici*." The mentioned periodical had circulated widely among practitioners within the German reich.

With respect to Jews in the insurance panel practice, it has been newly decreed that those Jews who have been allowed to continue in medical practice (under the restrictions described in previous letters) may now take part in panel practice among insured Jews and their families; a special permit is needed for panel practice.

That, actually, a definite lack of physicians has resulted from the suppression, since October 1, of Jewish doctors is evidenced by the recent establishment of "policlinic treatment centers" at seventeen municipal clinics of Berlin. These centers are designed for the exclusive use of members of sickness insurance clubs and patients referred by the social service agencies; in other words, just those groups which are usually treated by the panel practitioners. It was expressly stated that these auxiliary centers were designed to lighten the load

of the panel doctors (a new consideration). The medical staffs of fourteen municipal emergency stations were also increased for the same purpose as well as for emergency house visit duty, especially at night. Meanwhile it has been decreed that the foregoing measures shall be discontinued November 16.

#### ITALY

(From Our Regular Correspondent)

Nov. 15, 1938.

#### Registrations in Universities Limited

The minister of national education fixed the number of registrations in the universities of Rome and Naples for the year 1938-1939 at a maximum of 15,000 and 10,000 respectively. The action was taken to prevent a plethora of students and to make the theoretical teaching and laboratory work more profitable. The criteria to be followed in accepting applications for registration will be fixed by the personnel of the universities in agreement with the opinions of the minister of education. Residents in the city will be given the preference over nonresident applicants.

#### Treatment of Fractures of Limbs

Professor D'Agata of the University of Messina lectured before physicians of the army on modern trends of military surgery. He said that when reduction of a fracture cannot be done satisfactorily at a first aid station, especially in war, it is advisable to apply a Thomas or metallic Cramer splint or a similar apparatus for temporary immobilization. The good position of the fragments is controlled by x-ray examination. Application of large casts in which the proximal and distal joints are included is not advisable. Immobilization is applied only over the focus of the fracture, leaving the limb in a position of rest and, if possible, leaving all the joints free. These conditions can be obtained by traction with the limb, especially the leg, in a double-inclined plane. Adhesive plaster or a bandage with Unna's paste (zinc oxide, glycerin and mucilage) is resorted to when traction is applied to the soft parts. Direct traction on the skeleton can be done by means of wire (Kirschner and Klapp's method) or a nail through the calcaneus. The patient with a fracture of the leg is asked to do certain walking after consolidation of the immobilizing apparatus, as walking stimulates consolidation and prevents rigidity of the joint. For an open fracture some surgeons advise treating first the wound and then the fracture, whereas others follow the inverse order. In first aid stations it is advisable to limit the treatment to cleansing the wound, temporary immobilization of the limb without reduction of the fracture, and bandaging the wound. The patient is immediately transported to a surgical center so that he may have proper treatment during the first four or six hours after trauma.

#### Meeting of Academy in Florence

The Accademia Medico-Fisica of Florence recently met. Dr. Ferranti spoke on the value of electrocardiography in the diagnosis of coronary insufficiency. He said that only the monophasic wave and the coronary wave, which is a proper wave of myocardial infarct, are of precise diagnostic value. A Q<sub>s</sub> wave of the Willins type in patients with precordial pain shows the presence of Roemheld's syndrome rather than coronary insufficiency. It depends on a transverse position of the heart. A depression of the S-T segment or an inversion of the T wave may be due to hypertrophy of the right or the left ventricle. The simultaneous presence of other signs of predominance of either ventricle shows ventricular origin, whereas their absence shows coronary origin. The tests for diagnosis of coronary functions are of little value. The speaker advised a careful study of the electrocardiograms for a precise interpretation of diagnostic value.

Dr. Bretta said that he followed the behavior of the potassium-calcium ratio of the blood of normal persons after administration

of a large dose of insulin. Calcemia increased and potassemia diminished in disruption of the equilibrium of the sympathetic over the vagal stimulation. The speaker believes that the sympathetic disequilibrium is the cause of the disturbances of circulation of diabetic patients in the course of insulin therapy.

#### New Type of Malignant Granuloma

Professor Freund, in a lecture recently delivered to the Associazione Medica Triestina, spoke on a new type of Sternberg lymphogranuloma. He reviewed Oberling's classic experiments on leukemia in chickens and the identification of the virus in the disease. He reported three cases of grave fungoid mycosis, a case of lymphocytoma and a case of malignant lymphogranuloma of Sternberg's type. His case and two cases reported from France in 1917 form the group of cases of a new type of malignant lymphogranuloma which is generally called perioral eosinophilic granuloma.

### POLAND

(From Our Regular Correspondent)

Nov. 27, 1938.

#### Reaction of Physicians to the New Medical Law

As reported some months ago, the number of physicians in Poland is much too small in proportion to the total population. There is a remarkable want of medical service in the villages, as most of the physicians are concentrated in large cities. This fact has long been considered by the medical authorities. Some months ago a bill was passed by the Polish diet aimed at satisfying the health demands of the country, according to which every physician who graduates after April 1, 1939, will be allowed to practice in large cities only after he has practiced for two years in towns of less than 5,000 inhabitants. The law caused a strong reaction among physician and student organizations. A deputation of the general medical council, with its president, Prof. Mieczysław Michałowicz, received by the prime minister, claimed that the law will fail to obtain any positive improvement in the state of medical service in villages. Moreover, it will deter the youth from medical careers, as no financial aid for physicians obliged to practice in villages has been provided. Furthermore, the law will infringe on the right of every adequately qualified physician to practice anywhere in Poland. The students, in protest, stopped attending lectures for three days. The strike broke out last week in faculties of medicine all over Poland.

#### Organization of Medical Aid for Jewish Refugees

At the German-Polish frontier many thousands of Jewish refugees from Germany have been arrested by the Polish authorities. The refugees have lived under very bad hygienic conditions and have been exposed to undernutrition and atmospheric influences. The society for the health protection of the Jewish population in Poland, "TOZ," under the management of Dr. L. L. Wulman, has organized free medical aid for the refugees. A hospital was established at the frontier with an isolation ward for patients with infectious diseases and three infirmaries for outpatients. The staff consists of fifteen physicians. In the last weeks over 16,000 patients have been attended. There were 1,139 with influenza, 1,065 with catarrhal disorders of the respiratory tract, 829 with sore throat, 709 with rheumatism, 513 with peptic disorders, 349 with cardiac disorders and fourteen with mental disorders.

#### A New Medical School

When the question of obligatory practice in villages was taken up, the diet decided to take other measures to satisfy the demands for medical service and to raise the number of physicians. There are five universities with faculties of medicine, and the government proposed to establish a medical school in Lodz, a city of more than 500,000 inhabitants, which has

had no university. The project was welcomed by the inhabitants of Lodz, and a committee was organized to supply financial aid for the founding of the school. The antisemitic organizations of students of medicine in other cities, however, passed a resolution protesting against the establishing of the school, claiming that it would increase the percentage of Jews in the medical profession, since there are many Jews in Lodz and the committee is supported financially by Jewish philanthropists. This action of the antisemitic students is held by democratic groups to be a handicap in the supplying of sufficient medical aid to the country. In spite of it the building of the new medical school will begin shortly.

#### Treatment of Bronchial Asthma with Insulin Shock

Dr. Z. Askanas of Warsaw recently reported on the treatment of bronchial asthma by the method of Dr. Węgieńko, of Warsaw University, a method based on the observation that hypoglycemic shocks provoked by insulin control attacks of dyspnea in cases of bronchial asthma and diminish the disposition to recurrence. The effectiveness of the treatment is attributed not to the action of insulin itself but to the desensitizing effect of the hypoglycemic shocks. The author administered subcutaneously 40 units of insulin with the patient's stomach empty. The first manifestation of shock appeared in about forty-five minutes as a sensation of heat and a slight tremor of the hands. In from seventy to ninety minutes other features of shock appeared: tremor of the limbs, great hunger, profuse perspiration, a decrease in the pulse rate, a slight decrease in the arterial pressure and in the temperature and hyperreflexia. Sometimes the patient complained of palpitation of the heart or uneasiness. Great relief from the dyspnea was obtained soon after the early manifestations of shock had appeared. Some minutes later the dyspnea stopped entirely. The shock was stopped in from thirty to sixty minutes by the oral administration of large doses of sucrose solution, bread, honey, cakes and fruits. An immediate stopping of the shock can be obtained by intravenous injection of 20 to 40 per cent dextrose solution. To obtain improvement for a longer time, the author repeated the shocks every one to three days. The whole treatment consisted of from five to seventeen shocks.

In fifty-eight of sixty-five cases, great improvement was obtained. The attacks of dyspnea have not reappeared in from ten months to three years after treatment. Shock therapy failed to achieve permanent results when the bronchial asthma was associated with extensive pulmonary emphysema or serious endocrine disorders or was related to focal infection. There were seven cases of such asthma in the series. Shock therapy is the method of choice for asthma related to emotional disturbances, allergy, functional endocrine disorders and, especially, asthma in children. Even when permanent relief was not obtainable there was prompt control of the dyspneic attack in all cases.

## Marriages

THOMAS HAMILTON HOGSHEAD, Staunton, Va., to Miss Catherine Louise Gierhart of Yonkers, N. Y., in September.

AMOS GILMORE CRUMPLER, Fuquay Springs, N. C., to Miss Dorothy May Raine of Royersford, Pa., August 26.

FRANK RANDOLF PHILBROOK, Randolph, Mass., to Miss Madeline Hartford of Berwick, Maine, July 2.

ROBERT B. J. . . . . Ind., to Miss Ida Wood of Spencer in . . . . . 10.

THOMAS D. THOMPSON to Miss Martha Simons, both of Spokane, Wash., August 26.

RICHARD COLLINS JR., Waltham, Mass., to Miss Jean Chapman of Lincoln, August 26.

THOMAS E. BYRNE, Mentor, Ohio, to Miss Alice G. Mullen of Madison, Wis., recently.

## Deaths

**George Burgess Magrath**, Boston; Harvard University Medical School, Boston, 1898; member of the Massachusetts Medical Society; medical examiner of Suffolk County, 1907-1935; professor of legal medicine, emeritus, at his alma mater and at various times assistant in pathology, assistant in hygiene and instructor in legal medicine; was the first incumbent of a new chair of legal medicine established in 1932 at Harvard University, an appointment made on his twenty-fifth anniversary of service as county medical examiner; in 1934 the George Burgess Magrath Library of Legal Medicine at Harvard was dedicated in his honor; lecturer at the Lowell Institute; pathologist to the Long Island Hospital, 1898-1905, and the Carney Hospital, 1900-1905; co-author of "Studies in Variola and Vaccinia," 1903; aged 68; died, December 10, in Massachusetts General Hospital, Phillips House, of cerebral hemorrhage.

**Joseph Addison Crowell** Ⓢ Iron Mountain, Mich.; University of the City of New York Medical Department, 1881; fellow of the American College of Surgeons; past president of the Dickinson-Iron Counties Medical Society; formerly mayor, and member of the board of education; was chairman of an exemption board during the World War; aged 84; on the staff of the Iron Mountain General Hospital, where he died, October 22, of injuries received when he fell into the basement while the trap door was open.

**Richard Cecil Smith** Ⓢ Superior, Wis.; Washington University School of Medicine, St. Louis, 1911; member of the American Academy of Ophthalmology and Oto-Laryngology and the Pacific Coast Oto-Ophthalmological Society; fellow of the American College of Surgeons; ophthalmologist to St. Mary's, St. Francis and Good Samaritan hospitals; aged 52; died, October 30, of coronary occlusion.

**Louis Anthony Meraux**, New Orleans; Medical Department of Tulane University of Louisiana, New Orleans, 1904; member of the Louisiana State Medical Society; for many years sheriff of St. Bernard parish; at one time parish health officer; aged 58; died, October 6, in the Hotel Dieu, Sisters' Hospital, of coronary thrombosis, diabetes mellitus and carbuncle of the neck.

**Owen Taylor**, Kent, Wash.; Bellevue Hospital Medical College, New York, 1895; member of the Washington State Medical Association; fellow of the American College of Surgeons; served during the World War; on the staff of the Suburban Hospital, Auburn, formerly known as the Owen Taylor Hospital; aged 71; died, October 3.

**Arthur Alston Morrison** Ⓢ Savannah, Ga.; University of Georgia Medical Department, Augusta, 1923; fellow of the American College of Surgeons; chairman of the city council; on the staffs of the Warren A. Candler Hospital, St. Joseph's Hospital and the Georgia Infirmary; aged 38; died, October 17, of coronary occlusion.

**Jerome Francis Smersh** Ⓢ Owatonna, Minn.; University of Minnesota Medical School, Minneapolis, 1917; fellow of the American College of Surgeons; president of the board of health; served during the World War; aged 46; on the staff of the Owatonna City Hospital, where he died, October 26, of pneumonia.

**Richard Milo Olin**, East Lansing, Mich.; University and Bellevue Hospital Medical College, New York, 1899; member of the Michigan State Medical Society; state commissioner of health, 1917-1927; director of the health service, Michigan State College; aged 63; died, October 4, of coronary thrombosis.

**Charles Simpson**, Southbridge, Mass.; M.B., Laval University Medical Faculty, Montreal, 1903, and M.D. in 1904; member of the Massachusetts Medical Society; chairman of the board of health and school physician; on the staff of the Harrington Memorial Hospital; aged 61; died, October 12.

**Alfred Edwin Rhein**, Terre Haute, Ind.; Eclectic Medical Institute, Cincinnati, 1906; University of Illinois College of Medicine, Chicago, 1913; member of the American Academy of Ophthalmology and Oto-Laryngology and the Indiana State Medical Association; aged 55; died, October 21.

**William Humphrys Miller**, Terre Haute, Ind.; Northwestern University Medical School, Chicago, 1907; member of the Indiana State Medical Association and the American Academy of Ophthalmology and Oto-Laryngology; on the staff of the Union Hospital; aged 56; died, October 4.

**Japheth Edward Rawls** Ⓢ Suffolk, Va.; University and Bellevue Hospital Medical College, New York, 1899; fellow

of the American College of Surgeons; aged 63; medical superintendent of the Lakeview Hospital, where he died, October 14, of injuries received in an automobile accident.

**Alvin Raymond Moses** Ⓢ Charlton, Mass.; Tufts College Medical School, Boston, 1920; member of the New England Obstetrical and Gynecological Society; on the staff of the Harrington Memorial Hospital, Southbridge; aged 42; died, October 13, in a hospital at Worcester of pneumonia.

**John Manifold Wallace**, Lynn, Ind.; Medical College of Indiana, Indianapolis, 1903; member of the Indiana State Medical Association; served during the World War; aged 60; died, October 31, in the Randolph County Hospital, Winchester, of injuries received in an automobile accident.

**Robert Pillow**, Columbia, Tenn.; University of Pennsylvania Department of Medicine, Philadelphia, 1874; member of the Tennessee State Medical Association; at one time member of the board of education, mayor and health officer; aged 86; died, October 25, of pulmonary edema.

**Charles Dearborn McDonald**, Boston; Boston University School of Medicine, 1901; served during the World War; member of the Veterans' Administration; aged 63; died, October 20, in the Walter Reed General Hospital, Washington, D. C., of arteriosclerosis and heart disease.

**Arthur Churchill Shamblin**, Cartersville, Ga.; Grant University Medical Department, Chattanooga, Tenn., 1892; member of the Medical Association of Georgia; county commissioner of health; served on a draft board during the World War; aged 67; died, October 23, in Erick, Okla.

**Thomas J. Brown**, Grenada, Miss.; Memphis (Tenn.) Hospital Medical College, 1886; member of the Mississippi State Medical Association; city and county health officer; aged 76; on the staff of the Grenada (Miss.) General Hospital, where he died, October 10, of cardionephritis.

**William Kennedy Butler** Ⓢ Washington, D. C.; Columbian University Medical Department, Washington, 1882; professor emeritus of ophthalmology at the George Washington University School of Medicine; member of the American Ophthalmological Society; aged 81; died, October 17.

**John Webb Simmons**, Martinsville, Va.; Medical College of Virginia, Richmond, 1885; member of the Medical Society of Virginia; for many years county coroner; aged 79; died, October 13, in a hospital at Roanoke of hypertensive arteriosclerotic heart disease and nephritis.

**William Adam Wehe** Ⓢ Topeka, Kan.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1893; aged 69; on the staffs of St. Francis Hospital and the Stormont Hospital, where he died, October 1, following an operation for carcinoma.

**Ewan Alexander Robertson** Ⓢ Newton, Mass.; Chattanooga (Tenn.) Medical College, 1905; member of the New England Society of Psychiatry; medical superintendent and owner of the Woodlawn Sanitarium; aged 73; died, October 18, of coronary thrombosis.

**Charles Torrence Nesbitt**, Wilmington, N. C.; Baltimore Medical College, 1893; formerly city and county health officer, and health officer of Akron, Ohio; at one time surgeon in the U. S. Public Health Service reserve; aged 68; died, October 10, of myocarditis.

**J. Alphonse Sampite**, Cloutierville, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1902; member of the Louisiana State Medical Society; for many years member of the parish school board; aged 59; died, October 11, in New Orleans.

**Charles Edgar Smith**, Mart, Texas; University of Texas School of Medicine, Galveston, 1905; member of the State Medical Association of Texas; formerly secretary of the McLennan County Medical Society; aged 60; died, October 22, of heart disease.

**Thomas Lester Waggoner**, San Angelo, Texas; Baylor University College of Medicine, Dallas, 1930; member of the State Medical Association of Texas; health director of six districts; aged 34; was found dead, October 30, of a self-inflicted bullet wound.

**Willard W. Nye**, Hiawatha, Kan.; Jefferson Medical College of Philadelphia, 1877; member of the Kansas Medical Society; for many years county health officer; Civil War veteran; aged 92; died, October 19, of arteriosclerosis and myocarditis.

**Fred Bennett Colby** Ⓢ Gardner, Mass.; Dartmouth Medical School, Hanover, N. H., 1896; formerly city physician, and member of the board of health; on the staff of the Henry Heywood Memorial Hospital; aged 69; died, October 6, of heart disease.



**Arthur Shaw McDaniel**, San Antonio, Texas; Medical College of Ohio, Cincinnati, 1882; Bellevue Hospital Medical College, New York, 1890; member of the State Medical Association of Texas; aged 82; died, October 18, of chronic myocarditis.

**Donald Alpine McGregor** ☉ St. George, Utah; Barnes Medical College, St. Louis, 1903; fellow of the American College of Surgeons; medical superintendent of the Washington County Hospital; aged 62; died, October 11, of coronary thrombosis.

**Martin C. Bergheim**, Hawley, Minn.; University of Minnesota Medical School, Minneapolis, 1920; member of the Minnesota State Medical Association; aged 52; died, October 4, in St. Ansgars Hospital, Moorhead, of bronchopneumonia.

**John Maxson Brown Wainright**, Jersey City, N. J.; Columbia University College of Physicians and Surgeons, New York, 1904; on the staffs of the St. Francis and Fairmont hospitals; aged 58; died, October 20, of heart disease.

**Frederick Benjamin Schneerer**, Deadwood, S. D.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1903; veteran of the Spanish-American War; on the staff of St. Joseph's Hospital; aged 61; died recently.

**Frank Wesley Nagler**, Yakima, Wash.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1900; member of the Washington State Medical Association; aged 72; died, October 8, of heart disease.

**William Edgar Thomas**, Greensburg, Ind.; Medical College of Indiana, Indianapolis, 1901; member of the Indiana State Medical Association; aged 61; died, October 1, of angina pectoris, arteriosclerosis and hypertension.

**Frederick Capin Bowman**, Duluth, Minn.; Hahnemann Medical College and Hospital of Philadelphia, 1881; formerly member of the board of education; aged 89; died, October 4, of cerebral hemorrhage and hypertension.

**William Scott McKell** ☉ Chillicothe, Ohio; University of Colorado School of Medicine, Denver, 1913; on the staff of the Chillicothe Hospital; aged 55; was found dead, October 17, of chronic valvular disease of the heart.

**Stanislaus A. Bouvier**, Moosup, Conn.; Victoria University Medical Department, Coburg, Ont., Canada, 1889; aged 74; died, September 16, of arteriosclerosis, cerebral hemorrhage and chronic prostatic hypertrophy.

**Benjamin Kelly Simmons**, Blakely, Ga.; Atlanta School of Medicine, 1907; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1910; member of the Medical Association of Georgia; aged 68; died, October 7.

**Charles Chamberlayne Kingsley Phelps**, Sackets Harbor, N. Y.; Bellevue Hospital Medical College, New York, 1898; member of the Medical Society of the State of New York; aged 68; died, September 26.

**Theodore Toy Donaldson**, Powell, Ohio; Ohio State University College of Medicine, Columbus, 1929; member of the county board of health; aged 33; died, October 4, of coronary occlusion.

**John Pierre Nalbant**, Plymouth, Mich.; University of Michigan Medical School, Ann Arbor, 1928; aged 38; died, October 3, in the University Hospital, Ann Arbor, of carcinoma of the cecum.

**Avla Earl Snyder** ☉ Bryan, Ohio; Jefferson Medical College of Philadelphia, 1894; served during the World War; aged 69; died, October 20, in Crystal Lake, Mich., of coronary occlusion.

**Willard T. Nichols**, Milwaukee; Northwestern University Medical School, Chicago, 1894; member of the State Medical Society of Wisconsin; aged 73; died, October 22, of coronary thrombosis.

**Andrew Fletcher Weathers**, Shellman, Ga.; Vanderbilt University School of Medicine, Nashville, Tenn., 1894; member of the Medical Association of Georgia; aged 68; died in October.

**John Harvey Saylor** ☉ Marion, Kan.; Kansas City (Mo.) Medical College, 1904; county health officer; aged 72; died, October 17, in Christ's Hospital, Topeka, of mesenteric thrombosis.

**Ira T. Roberts**, Johnston City, Ill.; St. Louis College of Physicians and Surgeons, 1902; aged 59; died, October 26, in St. Andrew's Hospital, Murphysboro, of cerebral hemorrhage.

**Seine Bolks De Pree**, Sioux Center, Iowa; Rush Medical College, Chicago, 1903; served during the World War; aged 65; died, October 3, of carcinoma of the colon with metastasis.

**Stonewall Jackson Smock**, La Grange, Ky.; University of Louisville Medical Department, 1893; served during the World War; aged 72; died, October 1, of carcinoma.

**Louis Edward Dionne**, Ware, Mass. (licensed by years of practice); for many years chairman of the board of health; aged 74; died, October 16, of cerebral hemorrhage.

**Theodore C. Baumhauer** ☉ Uriah, Ala.; University of Pennsylvania Department of Medicine, Philadelphia, 1903; aged 58; died, October 9, of coronary thrombosis.

**Franklin Seymour Watterworth**, Detroit; Detroit College of Medicine, 1901; on the staff of St. Mary's Hospital; aged 61; died, October 5, of cerebral hemorrhage.

**Charles Henry Christian**, Austin, Texas; Meharry Medical College, Nashville, Tenn., 1914; aged 47; died, October 3, of uremia, chronic nephritis and myocarditis.

**George Averill Tolman**, Detroit; Medical School of Maine, Portland, 1893; aged 71; died, October 14, of carbon monoxide poisoning, self administered.

**John Edgar Rooks**, Shreveport, La.; University of Maryland School of Medicine, Baltimore, 1905; aged 63; was killed, October 18, in an automobile accident.

**George William Racey**, Park Hill, Ont., Canada; University of Toronto Faculty of Medicine, 1907; aged 56; died, October 13, in an automobile accident.

**Robert Mills Smith**, Camden, N. J.; Chicago Homeopathic Medical College, 1904; aged 71; died, October 30, of myocarditis and hypostatic pneumonia.

**William Marion Bryant**, Albany, Ga.; Meharry Medical College, Nashville, 1902; aged 64; died, October 11, in the Phoebe Putney Memorial Hospital.

**John Lee Lantz**, Kansas City, Mo.; Missouri Medical College, St. Louis, 1893; aged 74; died, October 20, in the Research Hospital of coronary thrombosis.

**Clifton B. Olds**, Chicago; Hahnemann Medical College and Hospital, Chicago, 1905; aged 72; died, October 31, following an operation for perforated ulcer.

**Thomas C. Nichols**, Falmouth, Ky.; University of Louisville Medical Department, 1873; aged 89; died, October 8, of diabetes mellitus and myocarditis.

**Kate E. Lozier**, Washington, D. C.; Columbian University Medical Department, Washington, 1895; aged 84; died, October 24, of bronchitis and pneumonia.

**John T. McMath**, Strong, Ark.; University of Arkansas School of Medicine, Little Rock, 1905; aged 58; died, October 26, of carcinoma of the lung.

**Orvis E. Biggs** ☉ Hot Springs National Park, Ark.; Barnes Medical College, St. Louis, 1908; aged 62; died, October 17, of coronary thrombosis.

**Ralph William Steele**, Fayetteville, Ark.; University of Arkansas School of Medicine, Little Rock, 1916; aged 48; died, October 8, of nephritis.

**John Folta** ☉ Ceylon, Minn.; University of Minnesota Medical School, Minneapolis, 1929; aged 37; died suddenly, October 14, of coronary sclerosis.

**Henry Stoesser**, Woodhaven, N. Y.; Eclectic Medical College of the City of New York, 1898; aged 76; died, September 26, of arteriosclerosis.

**Dennis Maxwell Smith**, Madsen, Ont., Canada; Queen's University Faculty of Medicine, Kingston, 1933; aged 30; died, October 30, of burns.

**Charles Franklin Spalding**, Springfield, Mass.; Columbus Medical College, 1886; aged 79; died, October 7, in the Wesson Memorial Hospital.

**John MacQuat Drew**, Lachute, Que., Canada; University of Edinburgh Faculty of Medicine, Scotland, 1911; aged 58; died, September 13.

**Warren J. Hall**, Oakfield, Ga.; Atlanta Medical College, 1885; member of the Medical Association of Georgia; aged 84; died, September 16.

**Alexander M. McCreary**, Poland, Ohio; Eclectic Medical Institute, Cincinnati, 1876; formerly mayor; aged 87; died, September 26.

**James Henry Roth**, Chicago; Rush Medical College, Chicago, 1895; aged 70; died, October 1, of cerebral hemorrhage.

**John Henry Cox**, Lucasville, Ohio; Eclectic Medical Institute, Cincinnati, 1889; aged 85; died, October 20, of senility.

**Marvin A. Nunn**, Halls, Tenn.; Memphis Hospital Medical College, 1901; aged 59; died, October 31, of pneumonia.

**C. J. Curry**, Benton, Ark. (licensed in Tennessee in 1889); aged 78; died in September.

## Bureau of Investigation

### THE INTERSTATE SERVICE

#### Exploiting Prescriptions for Complaisant Physicians

The vagaries of the mail-order business are axiomatic: now comes a concern known as the Interstate Service at 111 West Jackson Boulevard, Chicago, which appears to be writing to physicians with the hope of developing private prescriptions into nostrums. One paragraph of the promotional letter reads:

"How often have you thought of a favorite and unusually effective prescription that you would like to make available to the general public? One that could take its place with many of the proprietary preparations now generally on sale. Each of us cherishes some life long ambition and only the lack of opportunity prevents the fruition of long deferred plans. Ask yourself this question and determine right now whether any further delay is necessary."

This attempt to win doctors to commercial exploitation of their prescriptions is a strange type of seduction. Another section of the letter reads:

"Let each specialist keep within his field. And only by collaboration can the greatest good be achieved. We address you, a physician, as specialists in the field of mail-order selling. And, as such, we say that the cost of launching such a venture is moderate. You provide the formula. It is our business to help sell it for you."

And, as a final shot in the dark, the letter closes with the following plea:

"These are days when additional sources of income should not be overlooked. Why content yourself with a vague hope and a further promise to do something about that formula 'some day.' Please drop us a note requesting further particulars."

No reputable physician would, of course, lend his services, knowledge or personal treatment to such a performance. It is a peculiar form of stupidity that would lead a promoter to put out such an appeal at a time just after the new Wheeler-Lea and Food and Drug legislation have been passed. It is sad to think that there might be some physicians who would consider participation in such an unscientific and unethical venture.

### THE R. W. McCLINTOCK FRAUD

#### Research Laboratories Foundation Debarred from the Mails

"McClintock's Formula for Diabetes," "Sto-Bo-Ki" for "stomach sufferers" and "McClintock's Kidney and Bladder Sterilizer" were three mail-order fakes sold by a quack, one R. W. McClintock, who did business under the imposing trade styles "Research Laboratories Foundation" and "McClintock's Laboratories" at Ann Arbor, Mich. On July 14, 1938, the Postmaster General issued a fraud order closing the mails to McClintock and his two trade names. The information that follows is based partly on the memorandum of Hon. W. E. Kelly, acting solicitor for the Post Office Department, to the Postmaster General, and partly on material in the files of the Bureau of Investigation of the American Medical Association.

In 1933 the McClintock's Laboratories, then conducted from the Insurance Exchange Building, Detroit, was advertising ("for Adults Only") what were termed "60 Jewels of Life—A Safe and Effective 30 Day Treatment for Nerves and Glands Resulting in Happy, Normal Life." Price \$6.

In 1934 the McClintock fakery had moved to Ann Arbor and was featuring three nostrums: "Sto-Bo-Ki" for "stomach trouble," "Ex-Fre" for skin disorders and "McClintock's Whooping Cough Formula." At that time Sto-Bo-Ki was McClintock's *opus major* and testimonials with names and addresses were part of the advertising. Thus, Mr. Charles G. Lindner of New Castle, Pa., claimed to have cured himself of a long-standing case of duodenal ulcer with one bottle of Sto-Bo-Ki; Mr. Charles Estenberg of Detroit testified that he and his wife were both "completely cured of a bad stomach condition"; Mr. Donald Kirkendall, also of Detroit, claimed to have "entirely recovered" from "kidney trouble," from which he suffered for many years, after taking one bottle of Sto-Bo-Ki.

In 1936 Sto-Bo-Ki was being recommended as a cure for diabetes; later (1937-1938) McClintock was ballyhooing what he called his "Formula for Diabetes." The apparent discrepancy was cleared up by the analyses made by government chemists

for the Post Office Department; Sto-Bo-Ki the stomach remedy and McClintock's Formula for Diabetes were apparently the same thing! Each was found to be essentially a solution of free sulfuric acid and ethylsulfuric acid in alcohol flavored with cinnamon and ginger. In other words, the Aromatic Sulfuric Acid (Acidum Sulfuricum Aromaticum) of the U. S. P. and B. P. This may account for the claim made by McClintock in 1934 for Sto-Bo-Ki, before he decided to sell the same thing under two names for two widely different conditions. At that time he advertised Sto-Bo-Ki, in part, as follows:

"For this resultful remedy is the heritage of a family of famous physicians and chemists. The formula was discovered more than seventy-five years ago and is recorded in both the English and U. S. Pharmacopeia. More than twenty physicians and chemists, descendants of the discoverer, have guarded and handed down this precious formula from one generation to another. Today Robert McClintock, a direct descendant, controls the formula. This is STO-BO-KI, which is registered with the Pure Food and Drug Administration at Washington, D. C. . . ."

In a 1938 advertising leaflet McClintock declared that his "Formula for Diabetes" was "Registered with the United States Pure Food and Drug Administration and also the United States and British Pharmacopeias." In recent years McClintock developed caution in publishing what he declared were testimonials. No names or addresses were given other than such vague identification as "W.H.S. — Michigan," "K.C. — Georgia" and "L.I.H. — Pennsylvania."

McClintock is not a physician. According to the solicitor's memorandum McClintock claimed to be a chemist but no evidence appears in the record to substantiate the claim. McClintock also claimed—according to the memorandum—that he discovered the diabetes remedy (Acid. Sulf. Arom., U. S. P.) while his grandfather discovered Sto-Bo-Ki (also Acid. Sulf. Arom., U. S. P.)! McClintock offered no medical testimony in behalf of his nostrums but, as shown, did submit a number of testimonials. In this connection it is worth repeating what a former attorney general for the Post Office Department said a few years ago after having heard a large number of cases of medical mail-order fraud:

"Speaking generally it may be said that in all my experience in this office never has a medical concern, no matter how fraudulent its methods or worthless its treatment, been unable to produce an almost unlimited number of these so-called testimonials letters."

For a time McClintock had associated with him in what he claimed was an "advisory capacity" a Dr. C. B. Stouffer, who got out from under in March 1938. It was on April 29 that the Post Office officials served notice on McClintock to show cause why a fraud order should not be issued against him and his schemes. In fact, Dr. Stouffer's name was included in the list of those against whom the Post Office brought charges. According to the biographic files of the American Medical Association, Dr. Stouffer was born in 1878, received a diploma from the University of Michigan Homeopathic Medical School in 1913 and in the same year obtained licenses to practice in Michigan and Maryland. He is not a member of the American Medical Association. As Dr. Stouffer was no longer connected with McClintock's quackery when the fraud order was issued in July 1938, his name was not included in the order.

To physicians familiar with the pathology of diabetes and of stomach and duodenal ulcer (for which McClintock's nostrums

#### McClintock's Formula For Diabetes

Scientific — Ethical — Reliable

IT MAY seem strange to persons who have always heard and believed that there was no cure for Diabetes to learn now that McClintock's Formula for Diabetes never has failed in a single instance to give satisfactory results.

Just as the old theory of starving typhoid patients has been reversed through scientific research to feeding them, we, too, have found a new method of treating diabetes. This method is the result of years of scientific laboratory tests which have shown us that the presence of sugar in the urine is the result, and not the cause of diabetes. And upon this cause, we have spent a lifetime of investigation in our laboratories.

So science again has moved a step forward in the ranks of progress. It has revolutionized the old theory of the insulin needle and starvation, to regular diet and the readjustment of the digestive organs.

were recommended) the viciousness of the claims made for these products is obvious. But to those without medical knowledge the claim that the diabetic patient by using McClintock's nostrum could "eat a normal meal" and the further claim that the preparation "never had failed in a single instance to give satisfactory results" might readily lead to serious if not fatal results. The public once more has to thank the Post Office Department for protecting it against a cruel fraud by declaring that the McClintock scheme was one for obtaining money through the mails under false and fraudulent pretenses, representations and promises, and by closing the mails to it.

According to the evidence submitted at the Post Office hearing McClintock obtained his victims by "advertisements respecting his preparations being placed in various periodicals." The inevitable hook-up between certain publishers and quacks.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

PROBABLE BRAIN ABSCESS AND SYMPATHETIC MENINGITIS

To the Editor:—A sailor aged 23 was admitted to a hospital July 15, 1938, complaining of headache, fever and rigidity of the neck. The present illness started eight days before admission as persistent left-sided headache and moderate fever. The following day the headache became more intense and the fever higher; he had attacks of vomiting for two days and complained of rigidity of his neck and pain whenever he

Cerebrospinal Fluid Examination

	7/15/38	7/18/38	7/20/38	8/3/38
Color	pale yellow	pale yellow	colorless	colorless
Reaction	alkaline	alkaline	alkaline	alkaline
Clearness	turbid	turbid	clear	clear
Consistency	thin	thin with purulent clot	thin and delicate clot	thin
Total cells	6,300 per cu. mm.	4,300 per cu. mm.	350 per cu. mm.	35 per cu. mm.
Polymorphonuclears	87%	85%	32%	12%
Lymphocytes	10%	7%	62%	85%
Endothelial cells	3%	8%	6%	3%
Sugar	negative	slight (23.5 mg.)	38.2 mg.	51.8 mg.
Pandy test	heavy	moderate	moderate	trace
Chlorides		650.1 mg.	664.95 mg.	711.15 mg.

tried to bend his head and of pains in the lumbar region radiating to both lower extremities. Together with these symptoms he also noticed an increase of the purulent discharge from that ear. He had been having purulent discharges from both ears off and on for nine months. One year and five months ago he was accidentally struck in the head with a piece of lumber, which rendered him unconscious for two days. On regaining consciousness he had paresis of the left half of the body, which gradually disappeared almost completely after five months' treatment except for slight weakness of the left lower extremity. The patient was highly febrile (39.2 C., 102.5 F.) on admission but was conscious; tenderness was elicited at the exit of the cranial nerves; the neck was rigid; the knee jerks were exaggerated; Kernig's sign was positive. The ears showed central perforation of the drum membrane, about 2 mm. in diameter, with a slight purulent discharge. There was no sagging of the posterosuperior wall of the auditory canal and no mastoid tenderness. Hearing tests showed slight conductive deafness. The vestibular tests showed normal reaction to turning and caloric tests. Examination of the blood July 15 revealed total leukocytes 21,400 per cubic millimeter, neutrophils 84 per cent, lymphocytes 12 per cent, mononuclears 4 per cent, eosinophils 0, basophils 0. The urine was normal. Blood culture July 20 was negative. Culture from the cerebrospinal fluid July 18, July 20 and August 3 was negative. The report of an x-ray examination of the mastoids July 18 stated that no definite opinion could be given. Culture from the nasopharynx July 25 was negative for meningococci and positive for Staphylococcus albus and aureus and diphtheroids. Treatment consisted of repeated lumbar puncture, the administration of sodium salicylate and methenamine and hypodermoclysis with isotonic dextrose solution. The fever soon abated; four days after admission the patient was afebrile and has remained so ever since. The headache and rigidity of the neck rapidly disappeared. The discharge from the ear also rapidly decreased even though the ear was not treated. However, up to the present time (August 20) slight weakness and numbness of the left lower extremity has remained. I should like to know your diagnosis of the case. Failure to isolate any organism from the cerebrospinal fluid naturally made the diagnosis difficult and speculative. Is it a case of purulent meningitis of otitic origin? If so, how did the infection get into the subarachnoid

space? There were definitely no signs of mastoiditis, labyrinthitis or other septic focus in the temporal bone. The symptoms of meningitis were not preceded with pain and increased discharge from the ear. Don't you think that the purulent meningitis was probably due to organisms which entered the cranial cavity through the nose, as for instance meningococci? There are cases of the mild or abortive type of meningococcic meningitis in which I believe recovery may occur without serum therapy but by lumbar puncture only. Merritt and Fremont-Smith (The Cerebrospinal Fluid, Philadelphia and London, W. D. Saunders Company, 1937, p. 97) mentioned a case of meningococcic meningitis in which recovery occurred without any therapy except lumbar puncture. In the Philippines meningococcic meningitis is a comparatively uncommon disease and does not occur in epidemics.

A. S. FERNANDO, M.D., Manila, P. I.

ANSWER.—This patient suffered a severe head trauma, sufficient to render him unconscious, leaving in its train a hemiparesis and as an after-effect a muscular weakness in the left lower extremity. Eight months later a chronic purulent otitis media and meningeal symptoms developed: nuchal rigidity, high temperature and increased otorrhea. All of these also ran their course, with recovery taking place but leaving behind the same weakness in the left lower extremity. The diagnosis of a purulent meningitis can hardly be substantiated from the data submitted. Neither does the case history present any significant data on which to establish a diagnosis of meningococcic meningitis. The sequence of events that transpired may be reconstructed from the data given: From the trauma which this patient suffered there was formed a small blood clot which, by locally exerted pressure, accounted for the hemiparesis and the muscular weakness that remained afterward. Eight months later this encapsulated, partly organized clot became infected with the same organism which produced the purulent chronic otitis media. Thus there was formed an encapsulated brain abscess which conceivably "leaked" into the tympanic cavity and partly emptied itself in the discharge from the tympanic cavity through the perforation in the drumhead. The reactions noted in the cerebrospinal fluid are strongly suggestive of a meningeal tissue reaction, which is generally termed "meningitis sympathica." The second spinal tap, taken May 18, already shows a return of the carbohydrate content of the fluid, and the succeeding taps show this element increasing. Likewise the spinal fluid chlorides increased with succeeding spinal taps. This and the successive drop in the cell content are evidence enough of a meningeal tissue reaction which was in process of recession. The absence of bacteria in the fluid is further evidence of its nonpurulent nature. This observation of an abacterial fluid precludes the diagnosis of meningococcic meningitis as well as that of an otogenic streptococcic meningitis.

The case does not assume any of the aspects of a purulent meningitis of otitic origin. It more nearly approximates that of a meningeal irritation due to a secondarily infected blood clot, the latter produced by trauma. The brain abscess may be small. At present, from the description given in the inquiry, there is no sure evidence at hand to warrant the belief that the clinical course of this lesion has completely run its course. There may be subsequent developments which will require observation by both otologists and neurosurgeons.

CHRONIC DERMATITIS

To the Editor:—A white man, aged 43, complains of severe itching of the face. Burning and scaling occur daily regardless of the season but are more severe during hot weather. His present complaint dates back to 1924, when he was working in a gold mine in Idaho and noticed a rash on his forehead, which was treated as a sweat band rash with picric ointment. This condition was followed by a severe rash over the entire face; it was of the weeping type with slabs of yellowish matter peeling off and leaving raw, oozing surfaces. He was hospitalized and advised to have his teeth and tonsils removed. Following this he was sent to the Veterans' hospital. He remained there seven months, during which time multiple boils and abscesses developed. A culture was made and vaccine used to treat this condition. There is no history of syphilis and his past history is good. I have given him a series of Lederle's special pollen antigen and a course of autohemotherapy for possible allergic reaction to wild weeds. Can you advise any further treatment to alleviate this man's condition?

M.D., Nevada.

ANSWER.—Careful search for the etiologic basis in such cases is often without avail. Multiple sensitization following the severe picric acid dermatitis with infection seems likely and a neurodermatitis may have been added during the fourteen years of suffering. The summer exacerbations may be due to a reaction to some pollen present in the air, to increased perspiration or to untoward activity of the cholinergic side of the vegetative nervous system. Low diastolic blood pressure, high metabolic rate, rapid pulse and a tendency to flush and to sweat on slight provocation would bear out the latter suspicion. A thorough general examination, if not already made, should be done with special attention to the possibility of other foci

of infection in the gastrointestinal or genito-urinary tracts. The blood picture should be studied. Possible sources of reflex irritation should be sought.

Patch tests should be made on the skin adjacent to the area of inflammation with all substances that come in contact with the patient's face or that can be carried there by the hands. A small amount of the suspected substance is placed on the skin, covered by a small square of gauze fastened with tape, to avoid confusion of the reaction to the suspected substance with that so often seen to adhesive tape. If a dry substance, it can be moistened with water or better with the patient's own perspiration. No substance irritating to a normal skin should be used nor should any volatile substance be covered. The patches should be left on for two days unless severe itching occurs before that time. On removal of the patch it is well to mark the number of the patch on the skin so that a late reaction may be recognized. Inhalation tests may be made also, having the patient snuff up various dusts that are apt to contaminate the air he breathes and noting any exacerbation of the dermatitis that may follow. All positive tests should be repeated to rule out coincidence.

Whether or not such investigation succeeds in detecting the cause or causes of the dermatitis, local treatment is important. When the skin oozes or is acutely inflamed, cool wet dressings of aluminum subacetate solution, one part to sixteen parts of water, or calamine lotion or saturated solution of boric acid should be used. As the acuteness lessens, zinc paste applied thinly may be substituted, or a dry skin may do better with zinc ointment or even borated rose water ointment. Stimulating agents such as salicylic acid, resorcinol, crude coal tar, wood tars or sulfur must be used with caution. Before applying them to the whole affected area a patch test should be made or the proposed preparation should be applied to a small part of the inflamed area, which amounts to the same thing. Only after such application has proved harmless should the preparation be used generally.

Ultraviolet rays benefit some patients in this category, used locally and generally in suberythema doses. If the patient goes outdoors he probably gets all the ultraviolet radiation that is good for him. If roentgen rays have not been used they may afford great relief for a time, though the probability of a definite cure is slight. One-fourth erythema dose, 87 roentgens once a week for a few treatments, should bring relief if the dermatitis is amenable to this agent and in any event not over three or four full doses, 1,050 or 1,400 roentgens, should be given. The patient must be warned against repetition of roentgen treatment at any future date. For this reason it is preferable to save the roentgen rays for severe exacerbations resistant to other measures.

Sedatives such as bromides or phenobarbital may be of great assistance. Every effort must be made to restrict rubbing and scratching, for if this is not stopped no effect will be obtained from other measures. Mental treatment is of great importance.

Attempts to alter the balance of the vegetative nervous mechanism by autogenous blood injections or intravenous injections of solution of sodium thiosulfate may be helpful.

#### VASOMOTOR RHINITIS

*To the Editor:*—A girl aged 19 has been suffering from vasomotor rhinitis for the past year, the onset having been last July. Treatment has consisted of nonspecific protein (orally), calcium, nitrohydrochloric acid, belladonna, ephedrine and phenobarbital without noticeable effect. Local applications of various vasoconstrictors, such as ephedrine, epinephrine, benzedrine and neosynephrin give but temporary relief. She has been tested cutaneously for foods, epidermals and pollens, also for incidentals such as dust, kapok and orris root, with no positive reactions. A competent rhinologist confirmed the diagnosis but was unable to add anything further to the treatment. Physical examination and urine and blood tests reveal no deviation from normal except for atrophic chronic infected tonsils. Can you suggest any other treatment? Would there be a possibility that tonsillectomy might improve her condition?

R. HUGH WEISEL, M.D., Bowmanstown, Pa.

*ANSWER:*—In the absence of detailed information, it is impossible to say wherein the treatment could be improved. It would be helpful to know whether the skin tests for food were done by the scratch method or by the more sensitive intradermal method, always remembering that at best the number of positive reactions may not be over 25 per cent. Those using the intramucosal method report as high as 80 per cent positive results. The antigen is injected in minute amounts in the anterior end of the inferior turbinate. Lastly, no mention has been made of the leukopenic index test following food ingestion. The term "vasomotor rhinitis" covers a multitude of conditions. It would be necessary to know whether there

are polyps present and whether these are large enough to produce mechanical blocking of the nasal passages. It would be most important to see whether there is a true hypertrophy of the turbinates and the posterior ends of the inferior turbinates, hypertrophy of which would mean at least some degree of surgical intervention before the patient could be expected to breathe well through the nose. There remain a number of therapeutic methods regarding which there is some dispute but which in individual cases have offered some measure of improvement, including zinc ionization of the nasal mucosa, the injection of alcohol solutions beneath the mucosa of the turbinates, the similar injection of sodium morrhuate solutions and the blocking of nasal nerves with alcohol as advocated by Otto J. Stein in 1908 (Some Observations on Hyperesthetic Rhinitis, *Laryngoscope* 18:692, 1908) and others since. Hansel in his textbook "Allergy of the Nose and Paranasal Sinuses," St. Louis, C. V. Mosby Company, 1936, gives complete information about the treatment of this type of disease.

#### REMOVAL OF EXCESS HAIR

*To the Editor:*—In Queries and Minor Notes (THE JOURNAL, Dec. 25, 1937, p. 2161), regarding removal of hair from about the nipples in a woman aged 25, the answer states: "Electrolysis is the only approved method for permanent removal of hair." I should like to know what are the objections to the use of the coagulating current (high frequency) for the same purpose. Should the hair about the nipples be handled in a different way from that of the face? Please discuss electrolysis (with one needle and with multiple needles) and coagulation in the permanent removal of hair.

FRANCESCO RONCHESI, M.D., Providence, R. I.

*ANSWER:*—Although both methods mentioned require experience to remove superfluous hairs properly, electrolysis with the single needle method is usually a wiser procedure, associated with less local reaction and lessened danger of scarring. To remove hairs about the breast area with electrolysis, the procedure is much the same as that for the removal of hair about the face. While theoretically, there may be increased speed with the multiple needle method of electrolysis, practically it is much more difficult to control any variation in current by this method; scarring is more likely to supervene, and there is also more associated pain with the multiple needle method. All in all, the single needle method is the expeditious one, and a careful operator can accomplish as much with fewer complications and less discomfort to the patient by this method.

#### BRAXTON HICKS CONTRACTIONS, PENTOBARBITAL SODIUM AND STILLBIRTH

*To the Editor:*—A primipara aged 32 was delivered of a 6½ pound (3 Kg.) baby. Although heart beats (130) were heard until a few minutes before delivery, it was not possible to resuscitate the baby. Labor and delivery were normal. The second stage of labor was a little long, over one and one-half hours. Four and one-half grains (0.3 Gm.) of pentobarbital sodium was given and nitrous oxide gas was used to dull the pain. There was no toxemia during pregnancy; the kidneys were normal. The blood pressure was 94 systolic, 60 diastolic. The mother had contractions of the uterus for the last four or five months of pregnancy. Sometimes they were five minutes apart but usually twenty minutes, a half hour or an hour apart, day and night. There was no pain, although the uterus became tight. Could they have weakened the baby so that it could not stand labor? Could anything have been given to stop these contractions? Twelve years ago when the mother had an appendectomy her doctor told her she had an infantile uterus. She is a doctor's wife and was anxious to have her baby. If she becomes pregnant again, would you advise a cesarean section?

M.D., Texas.

*ANSWER:*—It is difficult to surmise the cause of death of the baby in the absence of a necropsy. Many babies who appear perfectly normal on external examination have serious congenital anomalies incompatible with life. The analgesia that the patient received could likewise have contributed to the fatal termination. Although the dose of pentobarbital sodium was not excessive, this drug combined with the administration of nitrous oxide tends to increase the incidence of asphyxia in the newborn with the resultant hazard of a fatal termination.

The Braxton Hicks contractions that occurred during pregnancy could not have been responsible for any possible damage. These contractions often become severe enough at the end of pregnancy to require some sedation and yet produce no harmful effects. It is hardly possible that they could have weakened the baby. Although progestin has been recommended for the relief of these contractions, its use would not have been indicated in this case. An infantile uterus likewise would not be a contributory cause. It is possible that such a condition would be a cause for sterility, but this patient had an uneventful pregnancy and labor.

If the patient becomes pregnant again, a cesarean operation need not be considered because of this recent experience. Her pelvis must be quite adequate, and this first labor was not at all abnormal in character. It would be well, however, to use analgesic drugs sparingly and perhaps substitute some drug for the pentobarbital sodium. It is unlikely that this unfortunate experience would repeat itself.

#### CARDIORENAL HYPERTENSION AND APOPLEXY

*To the Editor:*—A patient aged 56, 5 feet 5 inches (165 cm.) tall and weighing 185 pounds (84 Kg.), has suffered from hypertension of nephritic origin for the last ten years. He had a "stroke" Aug. 14, 1938, the right leg, right arm, the right side of the face and speech being involved. August 16 his right leg improved and he could raise his arm, but on August 17 he had another hemorrhage, the leg becoming bad again, the arm the same, and the speech became more "thick" and indistinct. He again showed improvement August 20 but developed an annoying hiccup August 22. At first I controlled it with an ice bag. Later on that was not enough. I tried sedation, belladonna, bromides and hyoscyamus, which did not help, so then I tried atropine. This controlled it, but when I paralyzed the vagus and controlled the diaphragm I lost control of the heart, and the pulse went up from 75 to 105. What would you advise me to do in this case? What is the prognosis?

HARRY HALLARMAN, M.D., New York.

**ANSWER.**—Hypertension with renal involvement, whether secondary or not, has an ominous prognosis. The occurrence of apoplexy implies, but does not prove, that there is considerable arterial degeneration. It is impossible to foretell whether renal decompensation, cardiac decompensation or another cerebral accident will terminate this man's life.

The management of his tachycardia can be guided only by data which are not available. With the acceleration of pulse following vagal paralysis there may have been changes in the arterial tension which would modify the suggestions. If his pulse does not become more rapid it might be wise to do nothing about it, for the time being at least. Attention to the renal aspects of the situation is of the utmost importance; particularly efforts should be continued to maintain the hemoglobin concentration of the blood at as high a level as possible. With the extensive paralysis the patient is of necessity quiet. Although he is grossly overweight, there is hardly justification in expecting weight reduction to accomplish anything. An adequate supply of dextrose for the myocardium is vitally necessary. Digitalis can be used if its effects are carefully watched; it does not cause an increase in the arterial tension. However, there is no evidence in the query that the relative tachycardia is a sign of myocardial exhaustion. Oxygen inhalation would tend to slow the pulse, but unless the situation gets acutely worse the present pulse of 105 hardly warrants its continuous administration.

#### LIGHTNING CLEANER

*To the Editor:*—An industrial cleansing fluid sold under the name of Lightning Cleansing Fluid, distributed by the Mortemoth Company, Milwaukee, has been causing rather distressing symptoms of nausea, epigastric pain, vertigo and drowsiness. I should appreciate a report of its contents with a statement as to its organic effects, temporary or permanent, if any.

M.D., North Carolina.

**ANSWER.**—The Mortemoth Company appears to manufacture or distribute a variety of cleaning agents, fumigants and insecticides. The product mentioned apparently is "Lightning Cleaner" for use in fur and lining cleaning. This product is referred to in promotional literature as "a balanced combination of cleaning solvents especially prepared for the fur trade." Further it is described as nonexplosive and without fire risk. Without knowing the exact composition it is inferred from the statement as to nonflammability that this cleaner contains one or more chlorinated hydrocarbons. Carbon tetrachloride is typical of the chlorinated hydrocarbons found in this type of cleaning agent. Manifestations mentioned in the query are somewhat characteristic of the action of chlorinated hydrocarbons. The symptoms suggest only comparatively minor injury but some chlorinated hydrocarbons are capable of producing direful and acute manifestations centering about damage to the liver. The clinical manifestations and associated pathologic changes are similar to those of acute chloroform poisoning—chloroform itself being a chlorinated hydrocarbon. No chronic form of the disease is known but persistent sequels from acute poisoning may arise. In view of the limited information furnished in the query and in view of the lack of precise analysis of the product in question, no definite stand can be taken as to either diagnosis or preventive measures, but the entire situation suggests an injurious action from chlorinated hydrocarbons calling for prompt preventive steps.

#### POSSIBLE NEUROSYPHILIS: TREATMENT

*To the Editor:*—In May 1937 a baker complained of insomnia, lack of ambition, numbness of the hands and feet (the latter especially if sitting still for some time or at night), sour eructation, not especially at meals, and belching gas. He also had an occasional dizzy spell after standing up. He has had these symptoms for several months. He had supra-orbital headaches for three weeks. One year earlier he had typhoid injections followed by sudden diplopia and internal squint of the left eye. In March 1937 an optometrist who examined his eyes told him that no improvement could be made in his lenses and that there must be some general toxic condition causing his double vision. The diplopia is worse in the evening after he becomes tired. The optic nerve and fundus are apparently normal. In 1933 he had ulcers of the mouth and tongue; in May 1936 all his teeth were removed because of abscesses and pyorrhea. He does not remember having any sores. His wife died in 1930 at 32 of myocardial failure and possibly hypertension. She has had two children, now 7 and 8 years old, whose blood tests are negative. There have been no miscarriages. The patient has slight receptive deafness of the left ear; his hearing has been defective for twenty years. He had carbuncles in 1928. Physical examination showed a blood pressure of 125 systolic and 95 diastolic. There were no other abnormalities in the heart, lungs or abdomen except that there was a slight general alopecia, the pupils do not react to light, and the right pupil is slightly irregular in contour and slightly larger than the left. He has had a thick yellow postnasal discharge for five years. The knee jerks are normal, equal bilaterally; there is no Romberg sign and no tremor. The Wassermann and Kahn reactions were 4 plus. Since the beginning of treatment he has had three courses of twelve injections each of 0.6 Gm. of neoarsphenamine alternating with injections of three courses of 1 cc. of bismuth subsalicylate. The first course of bismuth consisted of seven injections of 1 cc. (2 grains). The second course consisted of twenty-four and the third of fourteen injections. The bismuth subsalicylate was alternated with neoarsphenamine in continuous treatment. He has also had potassium iodide continuously since May 1937: 15 grains (1 Gm.) daily up to a few months ago, when it was increased to 24 grains (1.5 Gm.) daily. Under this treatment the double vision improved slightly. He still has a moderate amount of internal squint of the left eye, but the knee jerks are 4 plus and equal; there is no Romberg sign. The finger to nose test is negative. May 18, 1938, the blood Wassermann reaction was 3 plus, the Kahn reaction 4 plus. The first spinal fluid examination was made June 26. The colloidal gold reading was 0000000000, the Wassermann reaction 2 plus, Pandy's test questionable. There was no apparent increase in pressure, the fluid was clear in color and it contained one white blood cell per cubic millimeter. The patient is somewhat nervous and irritable; however, he has a steady gait and a clear mind and his memory is normal. 1. What further treatment is indicated? Has the patient neurosyphilis? 2. Does the colloidal gold or the globulin test or the positive spinal Wassermann reaction determine the presence of neurosyphilis? 3. Is trypanamide or mapharsen indicated here? 4. Is the patient considered Wassermann fast? If so, is Wassermann fastness of any significance? 5. How long do you believe this patient has had syphilis? Where are the lesions of syphilis in this case?

M.D., Connecticut.

**ANSWER.**—These questions are of the type that cannot be answered by yes or no, as some of them include problems of syphilology that require considerable discussion. Neither are the data given with regard to the patient sufficient to make the answers conclusive.

1. The patient has been given in a little over a year thirty-six injections of neoarsphenamine and forty-five injections of a bismuth compound and some potassium iodide, apparently followed by definite improvement. However, as some of the symptoms have persisted, it would seem advisable to continue the treatment with at least two more courses of neoarsphenamine and at least four more courses of a bismuth compound. Even though the spinal fluid examination is not conclusively positive, the diagnosis of neurosyphilis seems justifiable in view of the other manifestations. The spinal fluid was examined apparently after considerable treatment had been given, which fact may explain the type of spinal fluid report obtained. If the fluid had been examined before treatment was started, the report might have been strongly positive. The clinical signs are suggestive of neurosyphilis of the meningovascular type.

2. A spinal fluid examination to be adequate should consist of the following tests: a cell count done immediately at the time of the withdrawal of the fluid; a flocculation or precipitation test; a colloidal gold test; globulin, protein and sugar estimations, and a pressure reading. The cell count is the most significant single test done on the fluid in the examination for syphilis, with the serologic test and the colloidal gold test following in that order. The degree of positivity of the various tests creates the picture of the positive spinal fluid as being of mild, moderate or severe degrees of positivity. One spinal fluid examination, however, does not warrant deduction as to the degree of neurologic involvement in a given case. It is only by repeated spinal fluid examinations that the severity of the spinal fluid involvement can be accepted as authentic. For example, the typically parietic type of fluid in a patient who has mild or early signs of neurosyphilis does not mean that the patient has dementia paralytica or that later on he will develop it. The same idea is applicable to a negative spinal fluid in the



presence of suggestive clinical symptoms of neurosyphilis. Further treatment, with observations of the patient and several more spinal fluid examinations, are usually necessary to settle such an issue conclusively.

The presence of a positive globulin test with all other tests of the spinal fluid negative is of no significance. Similarly, a colloidal gold curve of the syphilitic or parietic type is of no diagnostic significance if all the other factors are normal. In brief, it is the ensemble of the degree of positivity or negativity of the tests that creates the picture of a negative or positive report.

3. Tryparsamide might be used to advantage in this case if examination of the eyegrounds shows no abnormalities. If tryparsamide is used it should be given in series of ten injections with a similar amount of a bismuth compound given concurrently. There should be a rest period of two months between courses. Mapharsen would probably not be any more effective than the other arsphenamines.

4. It is too early to determine whether this patient is "Wassermann fast," and the question as to whether he has neurosyphilis must be settled before the patient can be classified as "Wassermann fast." If the serologic reaction of the blood remains positive in a patient who has neurosyphilis, the use of the term "Wassermann fast" is not justifiable because the involvement of the nervous system is the explanation for the persistence of the positive serologic reactions of the blood. The term "Wassermann fast" is limited to those patients who have no clinical evidence of visceral or neurologic syphilis and who have a negative spinal fluid. It is a better practice to think in terms of the status of the syphilis rather than in terms of the status of the serologic reaction, because not infrequently a so-called Wassermann fast patient is in the process of developing manifestations of syphilis that will become clinically obvious if he is observed long enough. On the other hand, the occasional patient is encountered who will maintain a positive blood reaction for many years and never show clinical evidence of late manifestations of the disease.

5. It is impossible to guess the duration of the syphilis. The inference from the data submitted is that if this patient has neurosyphilis it is of the meningovascular type with the vascular involvement predominating.

#### LABYRINTHINE VERTIGO

*To the Editor:*—A white man aged 61 has had vertigo for the last two years. He has had three attacks lasting about a week. Ordinarily he is active and works hard but during these episodes of vertigo he is utterly incapacitated for at least a week. There is no syncope, scotoma or tinnitus. He says that it is usually on changing position, on arising in the morning particularly, that he experiences the most discomfort. His present attack is associated only with vertigo but his last attack a year ago was marked also by a violent headache, which he described as a "tightening and pulling sensation on the back of his head and neck." He had gonorrhea thirty years ago and some chronic gastrointestinal complaints, which were corrected by attention to diet and bowel hygiene. His appetite is good; he drinks a small cup of coffee and a glass of wine occasionally but uses no tobacco. He is well developed and well nourished, weighs 170 pounds (77 Kg.) and is 6 feet (183 cm.) tall. The eyes, ears and throat are normal. Some nasal obstruction is present as the result of a poorly performed submucous resection many years ago. The lung fields are clear. The heart is slightly enlarged to the left (0.5 cm.) and there is a transient systolic blow heard at the apex, which is not transmitted. His blood pressure has never been higher than 113 systolic. The diastolic pressure varies between 60 and 70. During the last seizure his blood pressure dropped to 96 systolic and 58 diastolic. The peripheral vessels are definitely sclerosed. The pulse is 60, hard, full and regular. Enlargement of the abdominal viscera is absent. The lower extremities are normal except for some varicosities. Two years ago at the onset of the illness the patient was seen by an internist, who had a complete work-up done on him. He was also seen by an ophthalmologist, an otolaryngologist and a neurologist. The results of these examinations were pooled and a diagnosis of arteriosclerosis of the labyrinthine vessels was made. He was placed on a diet, wine and coffee were forbidden, and iodides were given orally. At the time blood Wassermann, blood count, chemistry urinalysis and electrocardiogram were all negative. What other phases of this man's illness should be investigated? What else ought to be excluded? What form of therapy is best applicable? What is the opinion with regard to the use of strychnine, ephedrine and thyroid preparations in a case such as this? How long should the regimen be kept up if instituted?

M.D., Brooklyn.

*ANSWER.*—The symptom as described is suggestive of some labyrinthine irritation of one or both labyrinths. Its rotational character and its aggravation by sudden movements of the head would also point to the same cause. If the eyes were observed during the attacks, a mild rotatory nystagmus might be noticed. The unusually low blood pressure as well as the drop in the latter to 96 systolic during the attacks would also point to a circulatory disturbance in the labyrinths.

The statement that the otolaryngologist's report was negative does not indicate the type of examination done which proved to be negative. For instance, an audiometric reading of both ears which may show loss of hearing in the high pitch register, combined with a reduction in responses to the caloric test of the vestibular apparatus from the vertical canals (with the head in the upright position), may point still further to circulatory involvement in the labyrinth. The vestibular tests should be done in all cases of vertigo, as occasionally a perverted response may point to possible intracranial disturbance.

The observations in this patient, however, seem to point to a Ménière syndrome due to circulatory disturbance. Foci of infection such as the teeth and tonsils should definitely be eliminated.

Treatment should be directed toward keeping the blood pressure at a higher level. The drugs mentioned do not seem to possess any specific action for vertigo. If the attacks become more frequent, the Furstenberg regimen should also be instituted: elimination of sodium chloride from the diet and the administration of large doses of ammonium chloride 3 Gm. (45 grains) in six capsules with each meal three times a day. This is given for three days and skipped for two days. If relief is obtained this regimen may be carried on indefinitely.

#### ACRODYNIA OR INFECTION?

*To the Editor:*—A white boy aged 9, 4 feet 4 inches (132 cm.) tall, weighing 75 pounds (34 Kg.) is pale and thin. He had no definite area of discomfort but looked acutely ill. The temperature was 102.2 F., the pulse rate 110 to 120. Physical examination showed definite photophobia, normal eyesight, the inferior palpebral conjunctivae slightly injected on both sides. The ears, mouth and pharynx were normal. The tonsils were out. The lungs were clear and normal. There was tachycardia; no murmurs were present. The abdomen was soft, the spleen not palpable. There were no tender areas on the abdominal wall. The kidneys were negative to palpation. The skin was moist and pale. The hair was of light color. Neurologic examination showed no nystagmus; the abdominal reflexes were present. There were no pathologic reflexes and no tremor. There was active sweating. Blood pressure was 120 systolic, 70 diastolic. The patient's history included measles, chickenpox, pertussis, mumps, grip and allergy to several foods. The mother tells of the complaints of headache, fatigue, anorexia and pains in the leg muscles, which started a week before my visit and were mildly present during visit. The patient perspires chiefly during the day, even when at rest; he has no night sweats. The temperature has been above normal for a week, often going to 101 and 102. There is no trouble with breathing except during epistaxis and there is no history of cough or dyspnea during this illness. The patient has a tendency to scratch himself, but no exanthems or cutaneous blemish has been noted. The patient is bright in school but shy of playmates. He literally "wants to be alone"; he sleeps a lot and is relatively inactive for a boy of his age and weight. His constant companion is his radio, which he keeps at a low pitch. He likes a darkened room and quiet. His first urine examination showed 1 plus albumin, some white blood cells, phosphate crystals and some bacteria. Another specimen of urine two days later was negative except for some hyaline casts. Later specimens of urine were negative. The hemoglobin is 80 per cent (Sahli), red blood cell count 3,700,000, white blood cells 9,100, neutrophils 68 per cent, eosinophils 1 per cent, lymphocytes 24 per cent, mononuclears 5 per cent, myelocytes 2 per cent. The Wassermann and Kahn reactions were negative. Tuberculin tests were negative (intracutaneous method). The child was treated for eight days, during which time his temperature and pulse came down to normal and he became active. Follow-up was uneventful. The therapy was alcohol sponge baths for excessive temperature; ammonium mandelate 5 grains (0.3 Gm.) every three hours by mouth for urine disinfection. Cod liver oil and brewers' yeast tablets were given in large quantities. Fluids were forced during the days with high temperature. Later a high caloric soft diet was given. Was this just a mild infection of the genito-urinary system (probably pyelitis) or the not too well known Swift-Feer disease? What would be the latest therapy of the latter?

ROBERT SCHWARTZ, M.D., Jamaica, N. Y.

*ANSWER.*—Most cases of Swift-Feer disease, or acrodynia, occur between the ages of 6 months and 3 years, rarely after 6 years of age. The common symptoms of acrodynia are insidious onset, listlessness and apathy or irritability and restlessness. The child will no longer play or smile. The appetite is poor. There is little if any fever unless intercurrent infections develop. The hands and feet are pink or cyanotic, the changes being more marked in the fingers and shading off gradually toward the wrist; pain, itching and burning occur to a marked degree in them. Transitory rashes appear on the trunk and extremities which may resemble urticaria, measles or scarlet fever. The disease lasts for several months. Excessive perspiration is marked and macerates the skin. Desquamation of the palms and soles occurs at frequent intervals. The child is a picture of abject misery. Photophobia is usually present. There is definite weakness of the musculature. The systolic pressure rises even in small children to from 120 to 150. The pulse is fast. The deciduous teeth frequently fall out. Insomnia and



constant tossing about and rubbing of the hands and feet are present. Maniacal symptoms may occur. As the disease progresses, the patellar reflexes are lost.

Regarding treatment there is nothing specific, as the etiology is unknown. Large doses of sedatives are necessary to control the extreme restlessness, pain and insomnia. Soothing lotions are used on the skin. Atropine in large doses lessens the excessive perspiration. Frequent baths and proper mouth hygiene are necessary. The diet must be forced because of the severe anorexia, even gavage feeding occasionally being necessary. A high vitamin diet is indicated, particularly in vitamin B complex and D and liver. Some have advocated ultraviolet rays. Patients should be kept out of hospitals because of the great danger of intercurrent infections.

It would seem that the patient described did not have acrodynia because too many of the classic symptoms were absent. He apparently did not have pyuria, as this is rare in a boy of this age and the one pathologic urine might be found in any febrile condition. In febrile pyuria (pyelitis) the fever subsides some days before the urine clears up, which was the opposite in this case.

The symptom complex described could have been an ordinary grippal infection even without obvious respiratory involvement, or a mild typhoid or paratyphoid infection even without enlargement of the spleen, or even a mild rheumatic fever even without a heart murmur, or a rarer condition such as malaria or undulant fever.

#### ANGINA PECTORIS OR ANXIETY NEUROSIS

*To the Editor.*—A white man aged 38 complains of intermittent precordial pain and oppression radiating down the left arm and up the left side of the neck. He also complains of fatigue, lassitude and "lack of pep" and states that late in the afternoon and early in the evening he becomes sleepy. This has been going on with remissions for the last three years. Physical or mental activity do not seem to influence these complaints much. He is a WPA engineer and his duties require him to drive about 110 miles several times a week. His wife has an arrested case of pulmonary tuberculosis. He has three children alive and well. He uses tobacco in the form of cigars in moderation and alcoholic beverages in periodic sprints, although he states that at present he takes a cocktail only occasionally. He had "nervous breakdowns" at 15 and 24 and says that nervousness seems to run in his family. His appetite is usually good, although he has had some gastrointestinal distress, such as gas, bloating and occasional heartburn. He weighs 200 pounds (91 Kg.) and is 5 feet 11 inches (180 cm.) tall. His weight has come down 4 pounds (1.8 Kg.) in the last month (I have put him on a 1,200 calory reduction diet). His blood pressure has ranged from 160/102 to 130/88. The rest of the examination is essentially negative except for the heart, which shows a slight enlargement to the left and downward and also a moderate accentuation of the second aortic sound. There are no murmurs; the pulse rate is 82 per minute and is regular. The Kahn reaction of the blood is negative, as is urinalysis. A basal metabolism test taken recently was plus 13 per cent. The fasting blood sugar is 90. My impression was that of a mild or perhaps pseudo-angina, with a possible hyperthyroid condition, mild hypertension, obesity and psychoneurosis. I have had him on theophylline with ethylenediamine, 1½ grains (0.1 Gm.) three times a day after meals, elixir of phenobarbital 1 drachm (4 cc.) three times a day; glyceryl trinitrate 1/100 grain (0.00065 Gm.) if necessary, and his reduction diet. He has been on this regimen a little over a month with no apparent improvement in his complaints. He has considerable financial worries and now is worrying about his physical condition despite my assurances that he will probably outlive me. I have hesitated to use benzedrine sulfate tablets for his extreme lassitude because of his anginal symptoms and mild hypertension. Cessation of the phenobarbital does not improve this troublesome complaint. I would appreciate any suggestions you can give me as to diagnosis and treatment.

M.D., West Virginia.

*ANSWER.*—One cannot lightly dismiss the probability of angina pectoris. Unfortunately there is no positive method for proving or disproving such diagnosis. There are certain points in the history which throw some doubt on this diagnosis. The fact that the distress is uninfluenced by physical or emotional strain does not fall in line with angina pectoris. Anginal pain is far more often substernal than precordial. The failure of glyceryl trinitrate to give relief interposes another obstacle to a definite diagnosis of angina pectoris.

The hypertension plus a moderate cardiac enlargement justify a diagnosis of mild hypertensive disease, but a basal metabolic rate of only plus 13 per cent without tachycardia and with obesity and somnolence does not offer secure ground for a diagnosis of hyperthyroidism.

If one were to disregard the pain, it seems that a diagnosis of psychoneurosis, probably an anxiety neurosis, with mild hypertension would be quite justified. Indeed, the pain may be a part of the psychoneurosis. The background of nervousness adds weight to such an assumption.

It would seem logical to manage this case as an anxiety neurosis, at the same time guarding against anything that would be detrimental to angina pectoris.

The use of theophylline with ethylenediamine or one of the other purine base compounds should be continued because of its probable beneficial effect on the hypertensive heart disease, since compounds of this nature exert a mild diuretic and cardiac stimulating action. The general management of anxiety neurosis may be found in any good textbook dealing with the subject.

#### HIRSUTISM IN YOUNG WOMAN

*To the Editor.*—A woman aged 25 had a supravaginal hysterectomy two and one half years ago for chronic metritis and endometritis with menorrhagia, metrorrhagia and secondary anemia. The artificial menopause thus induced has been attended with some of the milder endocrine manifestations, but her general health has been good. In recent months she has noticed an increasing hypertrichosis or hirsutism, which is becoming conspicuous on the face and soon may interfere with her occupation as saleswoman. What is the latest knowledge about the arrest or correction of this condition? It is my impression that endocrine imbalance incident to the operation may be causative. In *THE JOURNAL*, Jan. 1, 1938, page 84, an abstract from the *Münchener medizinische Wochenschrift* reports the efficacy of an ointment containing estrogen in the treatment of ovarian dermatoses. Have you any report of the use of such a preparation in hypertrichosis in the female?

M.D., California.

*ANSWER.*—The inquirer speaks of this as an artificial menopause. If the operation was only a supravaginal hysterectomy, the woman does not have an artificial menopause but only cessation of menstruation as the result of removal of the uterus and its endometrium. To produce an artificial menopause, both ovaries must be removed or their function must be destroyed by x-rays, interference with their blood supply or other means.

The development of hypertrichosis or hirsutism on the face is a separate condition and bears no relation to the supravaginal hysterectomy except possibly indirectly. It is possible that the excessive preoperative uterine bleeding which this woman experienced and her hirsutism could have been influenced by a like cause; viz., disturbance of the adrenal cortex.

The excessive bleeding may have been due to a chronic pelvic inflammation or to a uterine fibroid. If these conditions are ruled out, one must consider the possibility of disturbance of any one or any combination of the four endocrine factors which are responsible for the normal menstrual cycle; viz., the follicle stimulating and the luteinizing hormones of the anterior pituitary and the estrogenic and luteal hormones of the ovary.

There are at least four endocrine conditions that may be responsible for masculinization of the female, of which hirsutism may be a prominent feature. The first of these is an adrenal cortex tumor or hyperplasia with consequent hyperfunction. Reichstein (*Helvet. chim. acta*, 19:223, 1936) isolated an androgenic hormone from the adrenal glands that stimulates the masculine characteristics in the male and masculinizes the female. He named this adrenosterone. Removal of cortical tumors in women have been followed by reversion to normal.

The second condition in which hirsutism may be an accompanying sign is pituitary basophilism. This condition is almost always associated with disturbance of the adrenal cortex, but the two syndromes differ sufficiently to indicate that while they may be related they are not identical.

The third condition that may produce hirsutism is an arrhenoblastoma of the ovary which contains male testicular tissue.

The fourth source of hirsutism may be a heterosexual gonadal rest in the parovarian gland, which, with the decline of the primary gonadal function, may take on fresh activity in the direction of the opposite sex. This is more apt to occur at the menopause.

It should not be difficult to rule out pituitary basophilism. An arrhenoblastoma should produce some evidences of masculinization, such as enlargement of the clitoris, masculine type hair growth and amenorrhea. Menstruation is excluded in this case since the operation, but because of the fact that this girl had excessive uterine bleeding it militates against a diagnosis of arrhenoblastoma. Hirsutism produced by reactivation of masculine rests in the parovarian gland usually occurs at the menopause and not in young women and again should be associated with amenorrhea.

The most probable diagnosis in this case is tumor, hyperplasia or hyperfunction of the adrenal cortex. A moderate degree of hirsutism in women is not uncommon. There are many young women who have heavy, coarse hair on their legs and forearms which they shave, a moderate hair growth on the lower part of the abdomen to the umbilicus and some on the upper lip and chin over the zygomatic arches. However, if the condition is pronounced, the adrenal glands may be visualized by roentgenograms made after injection of air into

the perineal fascial space. This procedure is of doubtful value unless a fairly large tumor is present, and it may be accompanied by sudden and alarming complications. Bilateral exploration of the adrenals through incisions in the upper posterolateral lumbar regions can be done, but this is a serious operation when no definite evidence is at hand.

There is no endocrine treatment available, for in these instances there is probably a hyperfunction to treat and unless the tumor, if present, or the offending gland can be partially removed, there is not much hope for success.

#### WHEAT GERM OIL IN THREATENED ABORTION

*To the Editor:*—I am anxious to give the wheat germ oil treatment for threatened abortions a fair trial, but on account of the expense of adequate doses many of my patients cannot afford it, and if it must be fresh and kept cold I often wonder whether my patients get a potent product when they do buy it. Can you outline a diet for pregnant women to use during the entire pregnancy so that they will not need any of this extra vitamin? What about wheat germ that is sold at the health counters?

C. E. CASWELL, M.D., Wichita, Kan.

*ANSWER:*—The use of wheat germ oil in the treatment of women who have repeated abortions has found favor with some clinicians. There is now considerable evidence to indicate that the addition of vitamin E is beneficial to some of these patients. There is less evidence as to the value of treating threatened abortions with vitamin E. Usually if symptoms of threatened abortion manifest themselves, particularly bleeding, pathologic changes have already taken place in the ovum or in the chorionic vesicle incompatible with the continuation of the normal gestation. The addition of vitamin E to the diet, therefore, should be instituted early in the pregnancy in cases of habitual abortion and can be continued to viability of the fetus. Wheat germ oil should be kept cold to prevent deterioration. Green foods, such as lettuce and watercress, milk and milk products, are rich sources of vitamin E. It has been suggested, however, that some individuals have difficulty in assimilating a sufficient amount of this substance from their diets so that additional vitamin E is advisable. The Council on Pharmacy and Chemistry has not accepted any claims for vitamin E for this or any other purpose.

#### PSEUDOHERMAPHRODISM

*To the Editor:*—I delivered a pseudohermaphrodite on March 14, 1938. The child is the ninth baby of American parents, the father being a lease worker in the oil field. Both parents are of average intelligence and the other eight children are all living and perfectly normal. The pregnancy was uneventful and delivery was accomplished easily and normally eight hours after onset and without laceration. The birth weight was 7 3/4 pounds (3,515 Gm.). The child is perfectly normal in every way except as to the genitals: On either side of the midline, occupying the site of the labia majora, is an area of wrinkled and creased scrotal skin, somewhat pouched, each containing a movable mass the size of an olive seed. These two areas merge over the pubic site, forming an inverted U shaped arrangement. Emerging from the lower curve or the inner curve of the U is a structure which a casual glance would call a penis. It is considerably larger than the normal penis of a newborn baby with well developed glans, about one third of which was covered with prepuce. A small meatal dent appears at the normal site of a penile meatus, but there is no urethra-like passage in the structure. This fact, with the small amount of prepuce, identifies the structure as a clitoris. It further occupies the site of the normally placed clitoris, being below the mons and where the anterior ends of the labia minora would join if they were present. The dark area lying posterior to the cliteropenile structure is covered only with mucosa and is so fragile that the merest touch will cause bleeding. It is kept constantly protected with petrolatum gauze. It looks as though a vagina had been completely turned inside out. Through a canal the urine comes freely. A fold of the mucosa-covered tissue conceals a sphincterless anal opening. Considering these two openings as opposite angles of a rectangle, the two remaining angles mark blind passages. The one opposite the anal opening, posteriorly, is about 1 inch deep and would receive the eraser end of a lead pencil. The anterior one is smaller both in depth and in diameter. About twenty physicians in the surrounding country have seen the child, and the consensus seems to be that we must await the adolescent development of sex and genital characteristics before even a tentative decision as to sex can be made. This being the case, how shall the child be denominated during that interim—Jim or Jemima? More important just now, however, is what can and should be done to cover and protect the skinless area, which is of considerable extent.

M.D., Pennsylvania.

*ANSWER:*—The description undoubtedly justifies the diagnosis of masculine external pseudohermaphrodisism as evidenced by the presence of a rudimentary vagina, transformation of labia majora into scrotal-like structures in which a mass, presumably testes, is palpable, and an elongated penis-like clitoris. Management of this case should largely depend on whether or not internal female sex organs are present. No mention has been made of whether or not a rectal examination reveals the presence of

internal female sex organs. If rectal examination is unsatisfactory, a pneumoperitoneum may be necessary to establish the presence of such organs. Finally, laparotomy may be justified as a final diagnostic measure. If the presence of ovaries is established, removal of both testes and plastic restoration of the vagina would be indicated. In this way a definite female tendency would be established. If no ovaries are to be found, it would seem wiser to leave the testes in situ and thus establish a definite male tendency. Operative details may be found in Hugh Young's book on pseudohermaphrodisism.

If no operation was performed, the possible presence of both male and female generative organs doubtless would lead to the pitiful picture of the fully developed intersex, combining both male and female secondary sex characteristics. Much consideration should be given to the time to be chosen for the operation. There is no doubt that a prepubertal operation would give much better chances as to final sexual development. The presence of functioning opposite gonads would definitely suppress such development.

As it seems desirable to establish a definite sex before onset of school age, an operation just before that time would seem desirable. At that time anatomic development is far enough along to establish a better diagnosis and facilitates delicate plastic surgery.

If, however, what appears to be a prolapsed vagina should give rise to inflammatory or other complications, surgical procedure at a much earlier date would be justified.

#### BLOOD IODINE DETERMINATIONS

*To the Editor:*—I am interested in instituting blood iodine determinations in connection with thyroid work. What method of procedure is most suitable to the needs of a relatively small diagnostic laboratory? It has been my understanding that most of the procedures now in use do not meet this specification, being both expensive and exceedingly complicated.

J. M. FEDER, M.D., Anderson, S. C.

*ANSWER:*—The determination of the content of iodine in the blood can now be performed in the clinical laboratory. A certain amount of practice and experience is necessary, however, before the results obtained can be used for clinical diagnosis. A clinical method, the result of ten years of hospital experience, has recently been reported (Matthews, N. L.; Curtis, G. M., and Brode, W. R.: Determination of Iodine in Biological Materials, *Indust. & Engin. Chem., Anal. Ed.* 10:612 [Oct. 15] 1938) which requires about three hours to make half a dozen blood iodine analyses. The special apparatus required costs about \$50 but it can be made by a good glass blower. The reagents are such that a single analysis costs about 12.5 cents. While it is true that in the past these methods have been expensive and quite complicated, this newer method is simpler and particularly adapted to the clinical laboratory.

#### DIVISION OF ILIOFEMORAL BAND

*To the Editor:*—I should appreciate whatever references you may have concerning the technic and indication for division of the iliofemoral band. This is sometimes called the Ober operation.

G. H. WISENER, M.D., Richmond, Ind.

*ANSWER:*—Complete details of the technic and indication for division of the iliofemoral band may be found in the following three articles:

Ober, F. R.: Back Strain and Sciatica, *THE JOURNAL*, May 4, 1935, p. 1580.

Ober, F. R.: The Role of the Iliotibial Band and Fascia Lata as a Factor in the Causation of Low-Back Disabilities and Sciatica, *J. Bone & Joint Surg.* 18:105 (Jan.) 1936.

Ober, F. R.: Relation of the Fascia Lata to Conditions in the Lower Part of the Back, *THE JOURNAL*, Aug. 21, 1937, p. 554.

#### PYLORIC STENOSIS IN GIRLS

*To the Editor:*—Lately I have heard two recent graduates from different medical schools say that pyloric stenosis in children is confined to boys. Since I had in the past two girls who were diagnosed as having pyloric stenosis in a large medical clinic, I should like to know whether this is at present the accepted opinion or whether it is the opinion of an individual investigator.

M.D., Pennsylvania.

*ANSWER:*—Pyloric stenosis is not confined to boys, but 80 per cent of the cases occur in males and 20 per cent in females. Sometimes the proportion is given as three to one instead of four to one. For further information on this subject consult the following references:

Abt, I. A., editor: Pediatrics, Philadelphia, W. B. Saunders Company 3:453, 1924.

Brenneman, Joseph, editor: Practice of Pediatrics, Hagerstown, Md. 3:11 (chapt. 5) 1936.

Griffith, J. P. C., and Mitchell, A. G.: The Diseases of Infants and Children, Philadelphia, W. B. Saunders Company, 1937, p. 561.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, Jan. 3-5 and June 20-22. Sec., Dr. J. N. Baker, 517 Dexter Ave., Montgomery.

ALASKA: Juneau, March 2. Sec., Dr. W. W. Council, Box 561, Juneau.

ARIZONA: Phoenix, Jan. 3-4. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: *Medical (Regular)*. Little Rock, June 8-9. Sec., State Medical Board of the Arkansas Medical Society, Dr. L. J. Kosminsky, 317 State Line, Texarkana. *Medical (Eclectic)*. Little Rock, June 8-9. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

COLORADO: Denver, Jan. 4-6. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT: *Basic Science*. New Haven, Feb. 11. *Prerequisite to license examination*. Address State Board of Healing Arts, 1895 Yale Station, New Haven. *Medical (Regular)*. Hartford, March 14-15. *Endorsement*. Hartford, March 28. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. *Medical (Hemorrhagic)*. Derby, March 14. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: Dover, July 11-13. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science*. Washington, Dec. 26-27. *Medical*. Washington, Jan. 9-10. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: Jacksonville, June 19-20. Sec., Dr. William M. Rowlett, Box 786, Tampa.

GEORGIA: Atlanta, June. Joint-Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

HAWAII: Honolulu, Jan. 9-12. Sec., Dr. James A. Morgan, 48 Young Bldg., Honolulu.

IDAHO: Boise, April 4-7. Dir., Bureau of Occupational License, Mr. D. B. Cruikshank, Rm. 355, State Capitol Bldg., Boise.

ILLINOIS: Chicago, Jan. 24-26. Superintendent of Registration, Department of Registration and Education, Mr. Homer J. Byrd, Springfield.

INDIANA: Indianapolis, June 20-22. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

IOWA: *Basic Science*. Des Moines, Jan. 10. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MAINE: Portland, March 14-15. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MASSACHUSETTS: Boston, March 14-16. Sec., Board of Registration in Medicine, Dr. Stephen Rushmore, 413-F State House, Boston.

MICHIGAN: Ann Arbor and Detroit, June 14-16. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 100 W. Allegan St., Lansing.

MINNESOTA: *Basic Science*. Minneapolis, Jan. 3-4. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Medical*. Minneapolis, Jan. 17-19. Sec., Dr. Julian F. DuBois, 350 St. Peter St., St. Paul.

MONTANA: Helena, April 4-5. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEBRASKA: *Basic Science*. Omaha, Jan. 10-11. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEVADA: *Reciprocity and oral examination*. Carson City, Feb. 6. Sec., Dr. John E. Worden, Capitol Bldg., Carson City.

NEW HAMPSHIRE: Concord, March 9-10. Sec., Board of Registration in Medicine, Dr. Fred E. Clow, State House, Concord.

NEW JERSEY: Trenton, June 20-21. Sec., Dr. Earl S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, April. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 23-26. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, 315 Education Bldg., Albany.

NORTH CAROLINA: Raleigh, June 19. Sec., Dr. William D. James, The Hamlet Hospital, Hamlet.

NORTH DAKOTA: Grand Forks, Jan. 3-6. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OREGON: *Basic Science*. Portland, Feb. 25. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

PENNSYLVANIA: Philadelphia, Jan. 3-7. Sec., Board of Medical Education and Licensure, Dr. James A. Newpher, 400 Education Bldg., Harrisburg.

PUERTO RICO: San Juan, March 7. Sec., Dr. O. Costa Mandry, Department of Health, San Juan.

RHODE ISLAND: Providence, Jan. 5-6. Chief, Division of Examiners, Mr. Robert D. Wholey, 366 State Office Bldg., Providence.

SOUTH DAKOTA: Pierre, Jan. 17-18. Director of Medical Licensure, Dr. B. A. Dyar, State Board of Health, Pierre.

VERMONT: Burlington, Feb. 14. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

WASHINGTON: *Basic Science*. Seattle, Jan. 5-6. *Medical*. Seattle, Jan. 9-11. Dir., Department of Licenses, Mr. Harry C. Huse, Olympia.

WEST VIRGINIA: Charleston, March 6-8. Sec., Public Health Council, Dr. Arthur E. McClue, State Capitol, Charleston.

WISCONSIN: Madison, Jan. 10-14. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

WYOMING: Cheyenne, Feb. 6. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

NATIONAL BOARD OF MEDICAL EXAMINERS  
SPECIAL BOARDS

Examinations of the National Board of Medical Examiners and Special Boards were published in THE JOURNAL, December 17, page 2328.

Illinois June-July Examinations

Mr. Homer J. Byrd, superintendent of registration, Illinois Department of Registration and Education, reports the written examination (graduates of foreign schools given also a practical test) held in Chicago, June 28-July 1, 1938. The examination

covered ten subjects and included 100 questions. An average of 75 per cent was required to pass. Three hundred and twelve candidates were examined, 307 of whom passed and five failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Arkansas School of Medicine.....	(1937)	81	
College of Medical Evangelists.....	(1938)	83	
Chicago Medical School.....	(1936)	81,	
(1937) 75, (1938) 78, 80, 80, 80, 81, 81, 81, 81,			
82, 82, 82, 83, 83, 83, 83, 83, 83, 83, 83, 83,			
84, 84, 84, 84, 85, 85, 85, 85, 85, 85, 85, 85,			
86, 86, 87, 88, 90			
Loyola University School of Medicine.....	(1936)	83,	
(1937) 83, (1938) 76, 78, 78, 78, 79, 79, 79, 79,			
79, 80, 80, 80, 80, 80, 80, 81, 81, 81, 81, 82,			
82, 82, 82, 82, 82, 82, 82, 83, 83, 83, 83, 83,			
83, 83, 83, 83, 83,* 84, 84, 84, 84, 84, 84, 84, 84,			
84, 84, 85, 85, 85, 85, 85, 85, 85, 85, 86, 86, 86,			
86, 86			
Northwestern University Medical School.....	(1934)	84,	
(1937) 80, 80, 83, 84,* (1938) 79, 79, 80,* 81, 81,			
82, 82, 82, 83, 84, 84, 84, 84,* 85, 85, 85, 85, 87,			
87, 88, 88, 88*			
Rush Medical College.....	(1936)	83,	
(1937) 78, 80, 80, 80, 81, 81, 81,* 82, 82, 82,* 83,			
83, 83, 83, 83, 84, 84, 84, 85, 85, 85, 86, 86, 87, 87,			
87, 88, 88, 88, 89			
School of Medicine of the Division of Biological Sciences.....	(1934)	85,	
(1937) 81, 82, 83, 83,* 84, 85*			
University of Illinois College of Medicine.....	(1938)	78,	
79, 79, 80, 80, 80, 81, 81, 81, 81, 81, 81, 82, 82,			
82, 82, 82, 82, 82, 82, 82, 82, 82, 82, 83, 83,			
83, 83, 83, 83, 83, 83, 83, 83, 83, 83, 83, 83,			
83, 83, 83, 84, 84, 84, 84, 84, 84, 84, 84, 84,			
84,* 85, 85, 85, 85, 85, 85, 85, 85, 85, 85, 85,			
85, 86, 86, 86, 86, 86, 86, 86, 86, 86, 86, 86,			
86,* 87, 87, 87, 87, 87, 87, 87, 88, 88, 90			
Indiana University School of Medicine.....	(1937)	82*	
Johns Hopkins University School of Medicine.....	(1935)	82	
Harvard University Medical School.....	(1937)	84	
St. Louis University School of Medicine.....	(1937)	81, 81	
Creighton University School of Medicine.....	(1937)	79	
New York University, University and Bellevue Hospital	(1934)	83	
Medical College.....	(1936)	82	
University of Pennsylvania School of Medicine.....	(1935)	81	
McHARRY Medical College.....	(1938)	81, 81	
Marquette University School of Medicine.....	(1937)	83,* 86	
University of Toronto Faculty of Medicine.....	(1937)	82	
McGill University Faculty of Medicine.....	(1936)	76	
Université de Paris Faculté de Médecine.....	(1936)	76	
Friedrich-Wilhelms-Universität Medizinische Fakultät,	(1924) 81, (1929) 78, (1934) 84,	(1936) 76, 80, 83	
Berlin.....			
Schlesische-Friedrich-Wilhelms-Universität Medizinische	(1926)	83	
Fakultät, Breslau.....			
Magyar Királyi Pázmány Petrus Tudományegyetem	(1926)	82	
Orvosi Fakultása, Budapest.....			
Regia Università degli Studi di Palermo. Facoltà di	(1929)	76	
Medicina e Chirurgia.....			
Regia Università degli Studi di Roma. Facoltà di	(1936)	76*	
Medicina.....			
..... Fakultät.....	(1935) 82, (1936)	81	
..... Fakultät.....	(1937)	78	
Universität Bern Medizinische Fakultät.....	(1937)		

School	Year Grad.	Reciprocity with
Chicago Medical School.....	(1922), (1937)	Arkansas
University of Michigan Medical School.....	(1937)	Dist. Colum.
Regia Università degli Studi di Bologna. Facoltà di Medicina e	(1936)	Penna.
Chirurgia.....		Michigan
Regia Università degli Studi di Roma. Facoltà di Medicina e	(1936)	Iowa
Chirurgia.....		Iowa

Thirty-six physicians were successful in the practical examination held for reciprocity and endorsement applicants in Chicago, June 30. The following schools were represented:

School	PASSED	Year Grad.	Reciprocity with
Univ. of Arkansas School of Medicine (1935), (1936), (1937)			Arkansas
Univ. of Michigan School of Medicine.....	(1918) Dist. Colum.		Dist. Colum.
..... School of Medicine.....	(1935)		Penna.
..... College of Medicine.....	(1936)*		Michigan
..... College of Medicine.....	(1935)		Michigan
..... College of Medicine.....	(1908)		Iowa
..... College of Medicine.....	(1935)		Iowa
..... College of Medicine.....	(1908)		Michigan
University of Michigan.....	(1934)		Michigan
St. Louis Univ. School of.....	(1937)*		Missouri
Washington University Sc.....	(1937)*		Missouri
.....			Nebraska
University of Nebraska College.....			Penna.
University of Buffalo School of.....			Oklahoma
University of Oklahoma School.....			Oregon
University of Oregon Medic.....			Penna.
Jefferson Medical College of.....			Penna.
University of Pennsylvania.....	(1928)*		Tennessee
McHARRY Medical College.....	(1937)		Tennessee
..... College of Medicine.....	(1935), (1937)		Texas
..... College of Medicine.....	(1934)		Missouri

School	PASSED	Year Endorsement of
College of Medical.....		(1937) N. B. M. Ex.
Northwestern Univ.....		(1934) U. S. Army
University of Kans.....		(1936) N. B. M. Ex.
University of Mary.....		(1906) U. S. Army
Columbia Univ. Col.....		(1930) N. B. M. Ex.
University of Buffa.....		(1932) N. B. M. Ex.

\* License has not been issued.

## Book Notices

**Nutrition and Diet Therapy: A Textbook of Dietetics.** By Fairfax T. Proudfit, Instructor in Nutrition and Diet Therapy, University of Tennessee College of Medicine, Memphis. Seventh edition. Cloth. Price, \$3. Pp. 923, with 64 illustrations. New York: Macmillan Company, 1938.

The plan of the seventh edition of this book remains the same as in previous editions. Section one has to do with normal nutrition. Section two includes a series of laboratory lessons in the preparation of foods and diets. Laboratory lesson two, for example, comprises a discussion of the composition, structure and place in the diet of the cereals, followed by a cooking demonstration. Lesson four concerns foods that are rich in energy, including the carbohydrates and fats; this chapter opens with a discussion of bread making and the use of fats in the diet, followed by a cooking demonstration, for which the students are advised to divide into two or three groups, each making biscuits or muffins. Section three takes up diet therapy. Here is a tabulation of the different kinds of routine hospital diets—liquid diets, soft diet, light, regular, high-residue diet, bland, smooth residue diet, low residue diet, no residue, high calory diets, low protein diets, high fat diets, and so on. These chapters pertain to diets for use in different diseases: diet in pneumonia and other fevers, diet in disturbances of the stomach, diet in constipation, in liver and gallbladder disturbances, in cutaneous and allergic diseases, in diabetes mellitus, in Addison's disease, in obesity, in pernicious anemia, in kidney diseases, in epilepsy, in arthritis, in deficiency diseases and in other conditions. Here also is a table giving the normal daily dietary standards for adults with modifications to meet the needs of the body in pathologic conditions. Section four comprises recipes for different kinds of beverages, fruits, cereals, salads, soups, sauces, meats, vegetables and desserts. The appendix contains information on food values. The book has been reorganized and rewritten to follow closely the curriculum of the National League for Nursing Education. This edition presents the latest methods of teaching the fundamental principles of nutrition in health and disease; it is a valuable guide for nurses, dietitians and others interested in nutrition and diet therapy.

**Of Yesterday and Tomorrow.** By E. O. Laughlin (Eolus). Cloth. Price, \$1.50. Pp. 108. Kansas City, Mo.: Brown-White Company, 1938.

Among medical contributors to poesy, Dr. E. O. Laughlin has had a welcome in many leading periodicals and newspaper columns. He has a flair for rhythm and his medical background gives color to all his verse. This is his most recent collection. He reveals humor and humane understanding. An example of his originality is the following epigrammatic clothing of a trite concept:

### SENESCENCE

This is old age's sorrow:  
That one no more may borrow  
From Tomorrow,  
And has so many debts to pay  
To Yesterday.

**Die Technik der Operation der Gaumenspalten und Gaumenlippenspalten nebst Ergebnissen.** Von Dr. Kurt Luhmann, Oberarzt der Chirurg. Univ.-Klinik Breslau. Paper. Price, 9.60 marks. Pp. 99, with 170 illustrations. Leipzig: Johann Ambrosius Barth, 1937.

This book presents in a clear and concise way the methods of Veau and of the author for the treatment of lip and palatine clefts. The rare forms of facial clefts are not in the purpose of the book. The author believes, with Veau, that the palate must be corrected when the child is beginning to learn to speak, that is, around the second year of life. He prefers to do the lip early, between 3 and 5 months of age, profiting by the softer skeletal frame. The preferred anesthesia is, in children and adults, ether by intranasal catheter or by the drop method. Children are prepared previously with atropine and avertin with amylene hydrate. He agrees with Veau that all the necessary elements to repair the defect are present. A complete cleft and its repair with the Veau method is clearly illustrated and described. For repair of clefts of the soft and hard palate, he has abandoned the Veau method except in particular cases because he considers it inconvenient in older children; the posterior palatine pedicle is not sufficiently freed; there is a

danger of dehiscence in the zone between the soft and the hard palate provoked by excessive tension, and the soft palate lacks the necessary freedom to allow an easy and sure closure. For these reasons he proposes a method of his own, derived from the original of Langenbeck and based on layer dissection of the cleft, bilateral section of the posterior palatine pedicle, debriding lateral incisions including soft and hard palate, complete mobilization and suture by layers of the flaps. His statistics are based on 177 patients, on whom he has performed 284 operations. After the 260th, he lost two cases. In using the method proposed by Veau for the closure of the cleft palate he has had some partial failures; otherwise his personal procedure has almost always been followed by success.

**The Infant: A Handbook of Modern Treatment.** By Eric Pritchard, M.A., M.D., F.R.C.P., Consulting Physician to the Queen's Hospital for Children, London. Cloth. Price, \$6. Pp. 744, with 52 illustrations. Baltimore: William Wood & Company, 1938.

Most books on therapy, after briefly presenting symptoms and diagnosis, offer several methods suitable for the treatment of each condition described. In this book, only enough information concerning the etiology and pathology of the various diseases is given to explain the rationale on which the treatment is based. A collection of many different methods of treatment is not presented, but rather only those methods which the author has selected because he believes them to be the best and most reliable. The reader is not left any choice as to what therapeutic procedure he should adopt. The book covers the disorders of the first five years of life. The complete index will enable the reader to find quickly the information he requires. The prescriptions appended also will be found useful. The treatment methods are practical and, in most instances, clearly presented in an amply detailed manner.

**Textbook of Zoology.** By George Edwin Potter, Ph.D., Professor of Zoology, Baylor University, Waco, Texas. Cloth. Price, \$5. Pp. 915, with 455 illustrations including 15 color plates. St. Louis: C. V. Mosby Company, 1938.

Not long ago, all that was known in zoology, botany, geology and related subjects was studied under the heading of natural history. With the rapid advance in science, zoology alone has grown to such magnitude that it must be divided into numerous special fields. The number of described species of animals is said to range from 840,000 to more than a million, and one writer has said that there are probably two million species of living animals, to say nothing of the large numbers of extinct forms. The subdivision of zoology which deals with the classification of organisms according to their natural relationships is taxonomy. This textbook classifies the animal kingdom after first giving a historical review of zoology, with brief biographies and photographs of some famous zoologists. Then follows a discussion of protoplasm and many other chapters, each devoted to some one phylum or class of animals. Chapter four deals with protozoa in general, chapter six with amebas, chapter seventeen with mollusks, and so on. Insects are the most abundant creatures on the earth, comprising more than 650,000 living species, many of which have never been seen by the majority of mankind. These arthropods have been on the earth, the author says, from the Pennsylvanian times of the late paleozoic era and have for probably a hundred million years been adjusting to a changing environmental complex. Their success is evident, for in a sense the two great contending forces today are insects and man.

The author has had the cooperation of several teachers and specialists in different fields in the preparation of many of the chapters. He has made an effort to lead the student to think of biology as related to mankind and to himself. This is more evident in the later chapters of the book, which take up the mammalia, where the interesting statement is noted that the camel's blood is an exception to the rule that mammalian blood contains unnucleated, circular red corpuscles. In the chapter on animal parasitism are discussions of many specimens that are parasitic to man. The later chapters concern wild life conservation, comparative embryology, genetics, comparative physiology, paleontology, and phylogenetic relations of animal groups and the theory of evolution. The many pages of glossary seem necessary in a science that has developed so fast.

**Traité d'électroradiothérapie.** Publié sous la direction de L. Delherm et. A. Laquerrière. Secrétaire général: H. Morel-Kahn. Secrétaire adjoint: H. Elschgold. Tomes I et II. Cloth. Price, 480 francs per set. Pp. 1,081; 1109-2015, with 450 illustrations. Paris: Masson & Cie, 1938.

These two volumes stand as a monumental work reflecting the interests of the French school of electroradiology. The entire work is dedicated to Professor Arsène d'Arsonval in tribute to his contributions in the application of physical science to disease. The majority of the ninety-two separate contributors are French; others are proponents of the French school residing in other European countries or in Canada. The subject matter begins with chapters giving the history and basic physical concepts of electrophysics as they have been applied in medicine. The underlying electrobiologic and radiobiologic concepts are fully discussed in reference to physical therapy and radiotherapy. The greater portion of this work is concerned with the different organ systems and the diseases therein which can be ameliorated or relieved by electrotherapeutic measures. In this respect the work is almost encyclopedic in extent. As a reference book it does not lack in completeness. As a textbook in electrotherapy and radiotherapy it will serve as a valuable guide to those familiar with the French language. The American reader will be struck particularly by the many diseases in which some form of electrotherapy is used. In this respect perhaps the work inadvertently suggests the long road of trial and error which has characterized so many attempts to apply electrotherapy or radiotherapy.

**Aids to Biochemistry.** By E. A. Cooper, D.Sc., F.I.C., A.R.C.S., and S. D. Nicholas, B.A., A.I.C., Lecturer in Chemistry, University of Birmingham. Second edition. Cloth. Price, \$1.50. Pp. 213, with 12 illustrations. Baltimore: William Wood & Company, 1938.

The sketchy text is intended to present the general principles of biochemistry to medical and science students who have already studied the subject by means of larger textbooks or lecture courses. It is "intended primarily for purposes of revision." It is also intended as a manual for experimental work. The work contains many inaccuracies. Among them are "the hexose molecules, for example, contain no less than four asymmetric carbon atoms" and "sixteen stereoisomeric aldoses are known." The treatment of the chemistry and importance of vitamins, of ketosis and antiketogenesis, male sex hormones, corpus luteum activity, enzymes, and acid-base equilibrium in the body is inadequate. The book would be of very little value as a "revision" for students of medicine in the United States.

**Focal Infection and Arthritis in the Light of Experiment.** By Ejnar Jarlöv, M.D., and Ove Brinck, M.D. Report from the Danish sections of the Association Internationale pour les Recherches sur la Parodontose and the Ligue Internationale contre le Rhumatisme. Paper. Pp. 94, with 22 illustrations. Copenhagen: Lassen & Stiedl, 1938.

After reviewing some of the earlier work on focal infection in arthritis, this little monograph, written in English, reports observations on experimental infection in rabbits. Streptococci of varying virulence were employed and it was found that strains of low virulence gave a greater infection percentage than those of high virulence. A measure of support is also given to the view that there are certain strains of streptococci with definite arthrotropic qualities. It is concluded that chronic joint disease which exactly resembles primary progressive polyarthritis (rheumatoid or atrophic arthritis) as well as osteo-arthritis can be produced experimentally on a purely infectious basis. As is well known, there are two schools of thought in this regard and these experiments definitely if not conclusively support the views of those who hold that rheumatoid arthritis and osteo-arthritis are not absolutely different and specific diseases. While there are some who believe that rabbits are entirely too obliging experimental animals for this type of experimental work, this report should be read by all those who are interested in this controversy.

**Der Operationskurs des Hals-, Nasen- und Ohrenarztes.** Von Prof. Dr. H. Beyer und Prof. Dr. A. Seiffert. Teil 1: Die Operationen am Ohr. Von Prof. Dr. H. Beyer. Second edition. Paper. Price, 24.50 marks. Pp. 278, with 317 illustrations. Leipzig: Curt Kabitzsch, 1938.

This brief yet comprehensive handbook of otologic surgery was planned as a guide for cadaver work as well as for the practicing specialist. The illustrations are new, clear and drawn from the original, occasionally international, sources. The explanatory text is accurate and simple, giving not only technical

details but also comparative statistics on various procedures. The author has brought his work down to date with the inclusion of Ramadier's and Lempert's paracarotid approach to the petrous apex, and of Holmgren's, Sourdille's and Wittmaack's operations for the relief of otosclerosis. More important, the usual operations are well illustrated with due regard to anatomic variations, and the technics suggested are those generally followed. There is a fair bibliography, as usual lacking reference to American work, and a brief subject index.

**Blodinamika proteidiv.** [By] N. B. Medvedeva. Pld redaktitsyu: O. O. Bogomoltsya. [Biodynamics of Proteins.] Paper. Price, 5 krb. 50 kopecks. Pp. 244. Kiev: Vidavnistvo Akademii Nauk URSR, 1938.

Nina Medvedeva is one of the most prolific research workers of the Ukrainian Academy of Sciences and claims to have separated a specific adrenal cortical hormone. The monograph at hand presents an extensive review of the chemical composition of proteins and their biologic properties. It is written in the Ukrainian.

**American Traumatic Guide.** [A National Survey in Compact Form of Traumatic Cases, Showing Physicians' Fees, Loss of Time and Percentages of Disability.] By William W. Bowen, M.D. Fabrikoid. Price, \$3. Pp. 80, with 23 illustrations. Des Moines, Iowa: American Publishing Co., 1938.

This is a compact survey of traumatic cases showing physician's fees, loss of time and percentage of disability.

The author has compiled charts and schedules in an effort to give physicians in general practice a reference that will help them in these situations. The schedules and percentages were compiled from reports of insurance companies, railroads, state insurance funds, United States Department of Labor and the experiences of specialists.

The first half of the book is purely anatomic. There is a glossary, definitions of terms used in the booklet and a report of workman's compensation, loss and extent of disability and by states.

The guide should be of value to surgeons doing casualty and compensation work and for claim superintendents, adjustments and legal and claim departments of insurance companies for setting up reserves and adjusting cases.

**Allgemeine Pharmakologie: Ein Grundriss für Ärzte und Studierende.** Von Dr. med. habil. Friedrich Axmacher, Dozent für Pharmakologie an der Medizinischen Akademie Düsseldorf. Paper. Price, 9.60 marks. Pp. 189, with 32 illustrations. Berlin: Julius Springer, 1938.

The author sees that general pharmacology is steadily replacing the old burdensome pharmacology with its immense number of drugs and recipes which the physician may rarely use. The object of the book is to present the general principles of pharmacology in a separate and short form, now lacking in the German language. The student may benefit from general pharmacology as much as from instruction in general pathology. The study must be pursued assiduously if the student is to gain fundamental conceptions of drug action. He discusses the absorption of drugs, their distribution in the body, excretion, relation of dose to effect, sensitivity of the organism, habituation, idiosyncrasy, fate of drugs in the body, synergism and antagonism, and chemical constitution in relation to action. The American student will find nothing new, either in method of presentation or in subject matter. All is to be found in the standard textbooks of pharmacology.

**Der Zyklus der Frau: Reform des Ehelebens.** Von Dr. Jules Samuels, Leiter der Einrichtung für Kurzwellentherapie, Amsterdam. Paper. Price, 4.50 guilders. Pp. 175, with 43 illustrations. The Hague: G. Naef, 1938.

The author of this book is trying hard to convince every one of his ideas. Within the last two years he has written three books and twenty-five articles in four different languages. Practically all the information imparted in this book is based on an instrument devised by the author and called a cycloscope. He first describes the anatomy of the pelvic organs. He then discusses endocrinology from a gynecologic point of view. There follows a description of the cycloscope, a simple instrument by means of which he claims he can study all the essential hormone processes in the body. By the use of this instrument, according to the author, it is possible for the first time to determine exactly when a woman ovulates. The author maintains that young girls and young women ovulate three times every month and that after a certain age or after a labor women ovulate

twice a month. Likewise the author claims that by means of this instrument it is possible to determine a pregnancy a few days after fertilization, even before a menstrual period is missed. Furthermore the instrument permits graphic demonstration of all ovulatory and menstrual disturbances. The essential part of the cycloscope is a spectroscope, and the purpose of the instrument is to study the reduction stripes of the oxyhemoglobin in the blood and the appearance of the first methemoglobin coloring. A great deal of the contents of the book are duplicated in another of the author's books, "Endogene Endokrinotherapie in der Gynäkologie," which was recently reviewed in *THE JOURNAL*. The author's claims are startling. Thus far no one has published any confirmatory reports, although the author says that Gauss of the Würzburg clinic, through his assistant Kastendieck, reported that he had investigated Samuels' cycloscopic methods of investigation and confirmed a few of his conclusions.

**Treatment in General Practice: The Management of Some Major Medical Disorders.** Volume II. Articles Republished from the *British Medical Journal*. Second edition. Cloth. Price, 10s. 6d. Pp. 436, with illustrations. London: H. K. Lewis & Co., Ltd., 1938.

This edition so soon after the appearance of the first is largely due to the application of sulfanilamide and similar compounds in the treatment of streptococcal and other infections. The thoroughly practical nature of this relatively small book by numerous authors on diseases of the respiratory tract, acute specific fevers and cardiovascular diseases makes it merit a place in the library of every practicing physician.

**Handbook of Physiology and Biochemistry.** By the late W. D. Halliburton, M.D., LL.D., F.R.C.P., and R. J. S. McDowall, M.D., D.Sc., F.R.C.P., Professor of Physiology, University of London, King's College, London. Thirty-fifth edition. Cloth. Price, \$5.50. Pp. 973, with 373 illustrations. Philadelphia: P. Blakiston's Sons & Co., Inc., 1937.

It is unusual for a scientific textbook to go into its thirty-fifth edition, which this handbook of physiology has done. It is still a popular book. The intervals between the last few editions have become shorter, although the number of books printed each time has been the same. New points have been added about the humoral transmission of the nerve impulse, vitamins, enzymes and sex hormones. The several sections on lymph formation, the pituitary, metabolism and diet have been completely remodeled. Some things which in former editions seemed important have been given less attention. The editors have kept in mind the needs of medical students preparing for examinations, and that accounts for some limitation of material and probably also for the popularity of the book. William S. Kirkes of St. Bartholomew's Hospital, a student of James Paget, edited the first edition in 1848. Kirkes thanks Sir James Paget for allowing him the free use of his lecture notes. With the fourth edition Mr. Savory, a lecturer on comparative anatomy and physiology at St. Bartholomew's, became the author. With the sixth edition came a new associate editor, Mr. Morant Baker, demonstrator of anatomy. In 1896, when a new edition was necessary, Professor Halliburton accepted the position, thus severing the long association between the book and St. Bartholomew's Hospital. The book now entered a new era of prosperity and in twenty-nine years seventeen editions were published.

**The Influence of X-Radiation on the Development of Immunity to Heterologous Transplantation of Tumors.** By Johannes Clemmesen. Denne Afhandling er af det lægevidenskabelige Fakultet antaget til offentlig at forsvares for den medicinske Doktorgrad, København. The translation into English by Robert Fraser. Paper. Price, 10 Danish kroner. Pp. 160, with 13 illustrations. Copenhagen: Levin & Munksgaard; London: Oxford University Press, 1938.

This small paper covered book will be valuable to those who are interested in the experimental phase of cancer work, because it contains a critical analysis of the experimental background as it applies to the transplantation of various tumors and also a detailed report of the author's own experiments. Clemmesen apparently inclines toward the genetic theory of cancer transmission and therefore appears to believe that mutation is perhaps the main factor in and the best explanation of most of the observations made in experimental cancer. To radiologists this report should be interesting because in his own experiments the author has used roentgen rays to a considerable extent in order to reduce the resistance of animals to transplanted tumors.

**Archiv und Atlas der normalen und pathologischen Anatomie in typischen Röntgenbildern. Der Kreuzschmerz in seiner Beziehung zur Wirbelsäule.** Von Priv. Doz. Dr. J. E. W. Brocher. Mit einem Vorwort von Prof. Dr. Volhard. Fortschritte auf dem Gebiete der Röntgenstrahlen, Ergänzungsband LV. Herausgegeben von Prof. Grashey. Paper. Price, 19.50 marks. Pp. 91, with 101 illustrations. Leipzig: Georg Thieme, 1938.

This interesting monograph on backache and sciatica contains discussions of anomalies of the spine, congenital defects, osteoporosis, lumbago and sciatica. It provides a clinical investigation of spina bifida, sacralization, spondylolisthesis and the gynecologic aspects of the subject. There is a foreign bibliography. The illustrations of vertebral pathologic changes are well done and highly instructive.

**Oftalmologia del paesi caldi.** Dal Prof. Vittorio Ruata, docente di patologia e Clinica oculistica nella R. Università di Roma. Cloth. Price, 45 lire. Pp. 362, with 96 illustrations. Milan: Ulrico Hoepli, 1938.

This comparatively small book deals with the ophthalmologic conditions encountered in practice in the tropical climates and is based on the personal experiences of the author. It is divided into nine chapters, five of which are devoted exclusively to the questions of oriental ophthalmology. The effects of intense heat and sunlight on the eyes are peculiarly tropical, as are the effects of the living conditions. To the ophthalmologists of the temperate zones, animal parasites are an almost unknown quantity, particularly the various forms of *Filaria*; but to the ophthalmologists in tropical countries the descriptions and illustrations that Ruata presents are of the utmost value. The chapters that deal with the bacteriology of the eye and the usual forms of conjunctivitis present nothing of unusual interest. A fairly long chapter is devoted to trachoma and offers a fairly good summary of the well known facts, except that the part devoted to treatment is rather skimpy. The diseases of the cornea and of the fundus again present the conditions that are peculiar to tropical ophthalmology. The final short chapter on surgery could well have been omitted. The black and white illustrations throughout are uniformly poor, except those depicting the various animal parasites. The colored illustrations, on the other hand, are uniformly good. Appended to each chapter is a good working bibliography. To one who reads Italian and who practices in tropical climates, the book is valuable.

**Dysmenorrhoea: Its Aetiology, Pathology and Treatment.** By Albert A. Davis, M.D., Ch.M., F.R.C.S., Hon. Gynaecological Surgeon to Outpatients, the French Hospital, London. Cloth. Price, \$4.50. Pp. 254, with 35 illustrations. New York, London & Toronto: Oxford University Press, 1938.

This subject, surrounded by so many theories as to both etiology and treatment, has been handled admirably by Davis in this treatise. The total amount of incapacity and the days of disability among women affected by dysmenorrhea each month are truly of vast economic as well as physical importance and more than warrant the attention which has been given the subject by many writers. Davis's book reviews the historical phases and the innumerable attempts at classification of dysmenorrhea. He finally sums up the latter as being symptomatically "spasmodic" and "congestive" or pathologically "primary" and "secondary." His summation along these lines is primarily for therapeutic reasons. He continues with an analysis of its etiology, including the hormone and neurogenic theories and a comprehensive discussion of the immediate causes of the pain. Nearly half the book is devoted to treatment, logically based on etiology as far as possible. For the cases requiring surgical treatment he gives in detail the technic of alcohol injection of the pelvic plexus and of resection of the presacral sympathetic nerve plexus, with excellent illustrations. The book is warmly recommended to the gynecologist and will prove of value likewise to the general practitioner.

**Paragilusniy tuberkuloz u doroslikh.** [By] N. S. Morozovskiy i D. P. Aleksandrovskiy. [Parahilar Tuberculosis in Adults.] Paper. Price, 3 krb. 50 kopecks. Pp. 139, with 22 illustrations. Kiev: Derzhamedvidav, 1937.

This is a monograph emanating from the Kiev Tuberculosis Institute. The monograph is a clinico-anatomic study dealing with hilus tuberculosis as the primary focus of tuberculous infection. It offers nothing that is not already known on the subject and is in the main a corroboration of the recent studies of Ranke. It is written in the Ukrainian.



**Clinical Roentgenology of the Digestive Tract.** By Maurice Feldman, M.D., Assistant Professor of Gastroenterology, University of Maryland, Baltimore. Cloth. Price, \$10. Pp. 1,014, with 358 illustrations. Baltimore: William Wood & Company, 1938.

This book covers completely the whole subject of roentgenology of the gastrointestinal tract. It represents a tremendous amount of work on the part of the author, not alone because of the large field it covers but particularly because of the enormous amount of reading the author has done, as is shown by the extremely large bibliography presented. The subject matter is covered completely and well. There are over 350 illustrations, a few diagrams, the rest reproductions of x-ray films, and almost 200 charts tabulating the reports of the numerous authors who are quoted. Dr. Feldman in his preface states that he is presenting a clinicoroentgenologic consideration of the gastrointestinal tract. This is borne out by the fact that each disease described has its clinical side presented sufficiently to allow both the clinician and the roentgenologist to obtain a fairly complete picture of the whole subject. Of course, this accounts for the size of the book. While this may have its good side, it seems that the clinical side could be condensed considerably without sacrificing its value. No attempt is made to decry the value of this work by calling attention to a few points. In describing the types of stomachs in their relation to the build of the individual it might be advisable to call attention to the work of Moody, who has shown in his study of a large number of students that there is frequently no conformity of the type to the build. Hurst and Stewart's book on duodenal ulcer is not referred to in that caption of the author's work, although references to Stewart do appear. Gastroscopists do not always find a relationship between the gastric folds observed gastroscopically and roentgenologically. It would seem in the last analysis that when the examination is not contraindicated gastroscopy should be the method of choice for diagnosis of gastritis and the character of the rugae. There are a few errors in grammar and in spelling of proper names in the first part of the book which were overlooked. One reference to peptic ulcer, described as gastric ulcer, was quoted wrongly since the type of ulcer described was actually duodenal. The book as a whole is well written, has a large index, and can be recommended for the use of clinicians and roentgenologists.

**20 rokov radyanskoj meditsini na Ukraïni.** Zbirnik za redaktsiynu O. O. Bogomoltsya, M. D. Strazhesko i S. S. Kagan. [20 Years of State Medicine in Ukraine.] Cloth. Price, 20 krb. Pp. 416, with illustrations. Kiev: Derzhavne Medichne Vidavnistvo, 1938.

This is a volume edited by the academicians O. O. Bogomolets, M. D. Strazhesko and Prof. S. S. Kagan and devoted to the development of medical service in Ukraine in the past twenty years. It is in the Ukrainian and unlike most contributions of this type is not accompanied by a synopsis in English, French or German. It deals with the development of public health and the growth of dispensaries, hospitals, sanatoriums and lying-in hospitals. One is impressed with the quantitative growth of medical service particularly in the fields of obstetrics, pediatrics and tuberculosis. It is difficult, if not impossible, to form an opinion from the contents of the volume as to the quality of the service.

**Outlines of Biochemistry: The Organic Chemistry and the Physicochemical Reactions of Biologically Important Compounds and Systems.** By Ross Alken Gortner, Chief of the Division of Agricultural Biochemistry, University of Minnesota, Minneapolis. Second edition. Cloth. Price, \$6. Pp. 1,017, with 165 illustrations. New York: John Wiley & Sons, Inc.; London: Chapman & Hall, Limited, 1938.

The second edition is of the same high standard of excellence as the first and needs no further recommendation as a useful book. The first third of the book is taken up with biophysical chemistry, including chapters on hydrogen ion concentration, oxidation-reduction, osmotic pressure and electrical conductivity, and the remainder on colloids. The rest of the book is on proteins, carbohydrates, including glycosides, lignin and tannins, plant and animal pigments, lipids and essential oils, hormones, vitamins and enzymes. These subjects are treated in a masterly manner and the book is very readable. For those who wish to use it for reference, however, it may be indicated that inositol, phytin and hexosephosphates are taken up with the compound lipids. Since the author does not include co-authors on the title page, we assume that he is

responsible for the entire text. It may be noted that on page 867 vitamin F is thrown out of the list on the ground of commercial exploitation. The reviewer has not noticed any lack of commercial exploitation of the other vitamins.

**Der Rheumatismus: Sammlung von Einzeldarstellungen aus dem Gesamtgebiet der Rheumaerkrankungen.** Herausgegeben von Professor Dr. Rudolf Jürgens, Stellv. Direktor der Universitätsklinik für natürliche Heil- und Lebensweisen, Berlin. Band VII: Rheumatische Kreislaufschädigungen. Von Dr. Siegfried Dietrich, Dozent für innere Medizin, II. Medizinische Klinik der Charité, Berlin. Mit einem Geleitwort von Prof. Dr. G. von Bergmann, Direktor der II. Medizin. Univ.-Klinik, Berlin. Boards. Price, 9 marks. Pp. 204, with 34 illustrations. Dresden & Leipzig: Theodor Steinkopff, 1938.

This monograph is one of the series on various aspects of rheumatism written by different German authorities. Dietrich has reviewed the literature on the effect of rheumatism, especially rheumatic fever, and on the circulatory apparatus and has expressed some of his own opinions. There is an excellent bibliography attached.

**Nervova sistema i vuglevodnyi obmin u bezkhibetnikh.** [By] M. V. Ermakov. Pld redaktsiynu O. O. Bogomoltsya. [Nervous System and Carbohydrate Metabolism of Invertebrates.] Paper. Price, 3 krb. Pp. 96, with 16 illustrations. Kiev: Vidavnistvo Akademii Nauk URSR, 1938.

The monograph by Prof. M. V. Ermakov in Ukrainian is concerned with the elucidation of the development in the phylogensis of the relationship between the nervous system and blood sugar level in a number of invertebrates. The author found that the nervous system begins to assume a role in the regulation of hemolymph sugar at that stage of evolution in which there appears in the nervous system a more or less differentiated sympathetic division. Such is the case in certain mollusks, lobsters, crabs, scorpions and insects. The monograph presents an interesting contribution to the problem of evolutionary physiology.

**Normale und krankhafte Steuerung im menschlichen Organismus.** Fünf- und zwanzig Vorträge gehalten in dem internationalen Fortbildungskurs der Berliner Akademie für ärztliche Fortbildung von 26. bis 31. Oktober 1936. Von Prof. Dr. H. W. Bansl, et al. Zusammengestellt von Professor Dr. C. Adam. Paper. Price, 12 marks. Pp. 302, with 39 illustrations. Jena: Gustav Fischer, 1937.

This is a collection of lectures about what we know at present concerning several subjects. Such subjects are included as the autonomic nervous system, endocrines, acid-base balance, central nervous system, psychic phenomena, sleep, circulation, nutrition, growth, allergy and inflammation. The essays are general in character and are not critical contributions to the subjects in question. Rather they are meant to serve as short reviews for the German practitioner to bring his information down to date. The volume will be of little or no interest to American physicians, since there are similar reviews in English.

**Biography of the Unborn.** By Margaret Shea Gilbert. Cloth. Price, \$1.75. Pp. 132, with 36 illustrations. Baltimore: Williams & Wilkins Company, 1938.

The author has attempted to present to the lay reader in intelligible terms the manner of the development of a fetus in utero. She relates this in the chronological pattern of the nine calendar months which comprise the normal period of human development before birth. She has succeeded in writing an interesting story of this complicated subject, although at times she is quite flowery in her descriptions and explanations. The illustrations greatly help to clarify the text. A relatively large proportion of our population is avid for factual and pseudo-factual information about the process of childbirth and many of these persons will find this book interesting and instructive.

**Kollapstherapie der Lungentuberkulose.** Herausgegeben von Walter Schmidt. Mit einem Geleitwort von Ludolph Brauer und Ferdinand Sauerbruch. In two parts. Paper. Price, 116 marks. Pp. 528; 531-1135, with 1,077 illustrations. Leipzig: Georg Thieme, 1938.

This is an elaborate work on collapse therapy in two volumes. The introduction by Ludolph Brauer and Ferdinand Sauerbruch in itself is a good recommendation for this work. Numerous authors have contributed chapters, and every phase of collapse therapy is discussed. The work of a number of American authors is cited, as well as of those from various other nations. These volumes are profusely illustrated and contain an extensive bibliography. They can be recommended to all physicians interested in collapse therapy.

## Bureau of Legal Medicine and Legislation

### MEDICOLEGAL ABSTRACTS

**Malpractice: When Judgment for Fee Does Not Bar Subsequent Malpractice Suit.**—McDowell, a licensed physician, sued Marchant to recover his fee for operating on Marchant's wife. Marchant filed a counterclaim, asking damages for a burn sustained by his wife, so he claimed, who, when on the operation table and while under the anesthetic, extended her hand and touched a hot radiator. The jury rendered a verdict for the physician for his fee but disagreed as to the counterclaim, whereupon the court "dismissed the counterclaim, but not on the merits." Judgment was then entered for the physician.

Later Marchant brought, in the city court of Buffalo, an action against the physician to recover damages for the burn sustained by his wife. The physician moved that the action be dismissed, relying on *Blair v. Bartlett*, 75 N. Y. 150, 31 Am. Rep. 455, in which the court said:

It must be considered as settled in this state, that a judgment in favor of a physician and surgeon for his professional services, rendered by a court of competent jurisdiction, in an action in which the defendant appeared and answered, setting up a defense which he maintained at the trial . . . is a bar to an action for malpractice by that defendant against that physician and surgeon for malpractice in rendering those services.

The facts involved in that case, said the court, differ essentially from those in this case. In the case cited, a complete trial had been had, a full opportunity had been given to the defendant to appear and defend, and a judgment was rendered. In the present case the jury considered two matters, the professional sufficiency and value of the services rendered by the physician and the alleged negligence of the physician in permitting the operating table to be too near the radiator. Obviously, the court said, the position of the operating table presented a problem which had attached to it no element of professional technic; it was a matter of commonplace negligence, involving no failure in subtle niceties of the performance expected and received from medical men as such. The jury, by reporting the disagreement in their verdict with respect to the counterclaim, indicated that they had reached no decision concerning the question. Marchant, then, has had no opportunity of having this essential phase of his case judicially determined.

The court believed, therefore, that Marchant should be given an opportunity to litigate the question as to the negligence "in this radiator propinquity circumstance" and therefore denied the motion of the physician to dismiss the action.—*Marchant v. Buffalo General Hospital* (N. Y.), 3 N. Y. S. (2d) 496.

**Compensation of Physicians: Liability of Employer for Medical Services Rendered Employee.**—Perry was seriously injured in the course of his employment. At the apparent suggestion of his employers that hospitalization was necessary, he was taken to a hospital in a neighboring town and the plaintiff physician called to attend him. After diagnosing Perry's condition, the physician visited the employers to ascertain who would be responsible for his bill and was assured that his bill "would be taken care of all right," that "the insurance company (with whom the employers carried a policy of workmen's compensation insurance) would take care" of it. The physician then undertook to care for Perry. Perry never instituted proceedings under the Missouri workmen's compensation act, to which the employers and the worker were subject, and the physician's bill was not paid. The physician then sued the employers at common law to recover his fees. The defendants contended that the court was without jurisdiction since the workmen's compensation commission of Missouri was the only tribunal authorized by law to pass on the matter. The court, however, sitting without a jury, entered judgment in favor of the physician and the defendants appealed to the Kansas City (Missouri) court of appeals.

Apparently proceeding on the theory that a physician could not have a claim for services litigated before the compensation commission independently of a claim for compensation filed by

the injured workmen, the court believed that to hold, as the defendants contended, that exclusive jurisdiction to pass on a physician's bill for services rendered an injured workman was vested in the compensation commission would permit employers, by settling with their injured workers without recourse to the commission, to defeat obligation for services rendered at the employer's request. Admittedly, said the court of appeals, Perry and his employers were operating under the provisions of the Missouri workmen's compensation act and Perry suffered an injury arising out of and in the due course of his employment. The employers, therefore, were in no position to assert that there was no duty on them to provide medical, surgical and hospital treatment. This duty would render them liable to pay a physician whom they called to care for their injured workman even though the rule of law is that when a physician is called at the mere request of a third party, on whom there rests no obligation to provide medical care, no contract to pay for the services is implied. Whether or not the employers in this case assumed an obligation to pay the physician was a question of fact for the trial court to determine and the court of appeals believed that sufficient facts were in evidence to support an inference that the employers had assumed that obligation. The court further believed that the fact that the employers expected the insurance company to pay would not alter the situation. The judgment in favor of the physician was accordingly affirmed.—*Gronoway v. Markham* (Mo.), 115 S. W. (2d) 136.

**Malpractice: Failure to Use Roentgenograms as Diagnostic Aid.**—The defendant did an open reduction of the patient's fractured ankle in November 1927, using a metal screw to keep the fragments in apposition. Seven years later, in November 1934, the patient again consulted the defendant, complaining of pain in the ankle that had been fractured. The physician, attributing the trouble to arthritis, wrapped the ankle with adhesive tape and adjusted an arch support which he had made for the patient at the time he reduced the fracture. About a week later he removed the adhesive tape. The ankle became more painful and finally, in January 1936, the patient went to another physician, who discovered through the use of roentgenograms that there had been some necrosis of the bone around the screw. The screw was removed and the patient made an uneventful recovery. Later the patient and her husband instituted a malpractice action against the defendant. The trial court at the close of the plaintiff's evidence directed a verdict for the physician, and the plaintiffs appealed to the Supreme Court of Arizona.

A physician to be liable for malpractice, said the court, must have done something in his treatment of his patient which the recognized standard of good medical practice in the community in which he is practicing forbids in such cases, or he must have neglected to do something which such standard requires. That standard must be shown by affirmative evidence and negligence on the part of a physician in departing from the standard must be established by expert medical testimony, unless the negligence is so apparent that a layman would have no difficulty in recognizing it. The testimony of other physicians that they would have followed a course of treatment different from that followed by the defendant is not sufficient to establish malpractice unless it also appears that the course of treatment followed deviated from one of the methods of treatment approved by the standard in the community. The treatment by the defendant in the present case, said the court, consisted of an "ordinary examination" of the ankle, the smoothing of an arch support which she was then wearing, the wrapping of the ankle with adhesive tape, and the removal of the tape about a week later. The only testimony bearing on medical standards or the treatment accorded the patient in November 1934 was that of the defendant himself and of the physician who removed the screw. The defendant testified that he did what was required by the patient's condition as it existed when he treated her in November 1934. The other physician could not state how long prior to January 1936 the screw should have been removed. He stated however that, if the ankle had been in the same condition in November 1934 as it was when he operated in January 1936, the screw should have been then removed but that it was impossible for him to testify as to when the condition justifying the removal

arose. He further stated that if he had been in the position of the defendant when the patient called in November 1934 his conclusion, like the defendant's, would have been that arthritis in the ankle joint was causing the pain but that he would not have been fully satisfied without having a roentgenogram made of the ankle. He further testified that the method of uniting fragments of bone used by the defendant was a standard one and that the screw was not removed, as a rule, unless it made trouble.

The plaintiffs based their claim of negligence almost entirely on the failure of the defendant to take a roentgenogram of the patient's ankle in November 1934. They urged that a failure to do so was such obvious negligence that even a layman knows that it was a departure from the proper standard. The Supreme Court, however, could not agree with this contention. It is true, said the court, that most laymen know that roentgenograms usually offer the best method of diagnosing physical changes of the interior organs of the body, and particularly of the skeleton, short of an actual opening of the body for ocular examination, but laymen cannot say that, in all cases in which there is some trouble with the internal organs, it is a departure from standard medical practice to fail to take a roentgenogram. In view of the testimony in the present case as to the arthritis from which the patient was suffering and which the second physician testified would have been his first thought as to the cause of the patient's pain in 1934, the court thought it was going too far to say that the failure to take a roentgenogram at that time was so far a departure from ordinary medical standards that even laymen would know it to be gross negligence. Since there was insufficient evidence in the record to show that the defendant was guilty of malpractice, the trial court properly directed a verdict for the physician. The judgment in favor of the physician was accordingly affirmed.—*Boyce v. Brown (Ariz.)*, 77 P. (2d) 455.

**Hospitals: Criteria of Charitable Status of a Hospital.**—If the purpose of an institution, said the Supreme Court of Arizona, is one which is recognized in law as charitable, and if it is not maintained for the private gain, profit or advantage of its organizers, officers or owners, directly or indirectly, the institution is properly characterized as a charitable one, notwithstanding the fact that it charges for most, if not all, of the services which it may render, so long as its receipts are devoted to the necessary maintenance of the institution and the carrying out of the purpose for which it was organized. The extent of the free services rendered by a hospital offers no adequate test of the charitable status of the hospital, the court said.

In the present case a baby was burned by negligent exposure to a hot water bottle in the appellant hospital. The contention that was advanced on behalf of the infant, in a suit against the hospital, was that even if it should be admitted that the hospital was a charitable institution, nevertheless it was bound to use due care in the selection of its employees and if it failed to do so it is liable for the negligence of such employees. The court, however, was unable to discover any evidence in the record sufficient to bring the case within the rule correctly stated in the contention. There was nothing to show which particular employee was guilty of the undoubted negligence which caused the injury. The record did show that three weeks prior to the injury in the present case another baby was burned in a somewhat similar manner, but this evidence was considered by the court entirely insufficient to establish that, even assuming that the same nurse was responsible for the two injuries, the hospital did not use due care in her selection and retention. It is true, the court pointed out, that the doctrine of *res ipsa loquitur* is properly applicable in such circumstances. But, the court continued, it was shown in the present case that all the nurses employed by the hospital were authorized by the state of Arizona to practice their profession. Where it is shown by positive evidence that the nurses employed by a hospital are of this character, any presumption that may have arisen from the doctrine of *res ipsa loquitur* that the hospital has not used due care in the selection of a given employee is destroyed, and in order to overcome such evidence there must be at least an affirmative showing that the hospital had knowledge of the previous negligence of the nurse and, notwithstanding such

knowledge, continued her employment. Since there was no evidence that the hospital ever knew that any one of its nurses was not competent in all respects, and since the record showed affirmatively that the hospital was, within the true meaning of the phrase, a charitable institution, it was not legally responsible for the unfortunate situation involved in the present case. The judgment of the superior court against the hospital was therefore reversed and the case remanded with instructions to enter judgment for the hospital.—*Southern Methodist Hospital and Sanatorium of Tucson v. Wilson (Ariz.)*, 77 P. (2d) 458.

**Workmen's Compensation Act: What Constitutes a Hernia.**—The claimant in this case contended that in the course of his employment he fell and immediately experienced a sharp pain in his left groin. He reported the accident to his foreman and was referred to the first aid station. What was found there is not shown by the record, but the claimant applied for compensation, alleging that an inguinal hernia had resulted. From an order of the workmen's compensation commission reversing an award that the deputy labor commissioner had entered in favor of the claimant, the claimant appealed to the Supreme Court of Michigan.

At a hearing before the deputy commissioner a physician who had examined the claimant a few days after the alleged accident and again about two months later testified that he had found on both occasions a left indirect inguinal hernia. On behalf of the employer, however, a physician who had examined the claimant in the interval between these two examinations testified that he had found an enlarged inguinal ring on each side, the ring on the left side being somewhat more enlarged than that on the right, but that he found no hernia. The condition that he found might be referred to, he said, as a potential hernia, but in his opinion nothing is a hernia unless there is a protrusion of a viscus or organ from its natural cavity. There was no protrusion of a viscus in the present case, although there was "a sharp mass by inserting your fingers in the rings and getting up on to the abdominal cavity." Some men, said this witness, call any such sharp mass a hernia, but others refuse to call it a hernia until after it has descended. In this case, in the opinion of this witness, the viscus had not descended through the rings.

Quoting its own decision in *Robbins v. Original Gas Engine Co.*, 191 Mich. 122, 157 N. W. 437, 438, the court said that in that case—

All the experts seem to agree that the visible evidence of the hernia is the protrusion through the inguinal ring of the peritoneum and its contents; "the hernia is the peritoneum going through, accompanied by the intestines or some other substance."

In the present case, said the Supreme Court, there was no protrusion through the internal inguinal ring and the evidence sustained the finding of the Commission on Labor and Industry holding that the claimant had a potential hernia or a predisposition to hernia. The order of the commission denying compensation was affirmed.—*Cessante v. Ford Motor Co. (Mich.)*, 278 N. W. 671.

## Society Proceedings

### COMING MEETINGS

- American Academy of Orthopedic Surgeons, Memphis, Tenn., Jan. 15-19.  
Dr. Carl E. Badgley, 1313 East Ann St., Ann Arbor, Mich., Secretary.
- American Association for the Study of Neoplastic Diseases, Baltimore, Dec. 28-30. Dr. Eugene R. Whitmore, 2139 Wyoming Avenue N.W., Washington, D. C., Secretary.
- American Student Health Association, New York, Dec. 29-30. Dr. Ruth E. Boynton, Students Health Service, University of Minnesota, Minneapolis, Secretary.
- Annual Congress on Industrial Health, Chicago, Jan. 9-10. Dr. C. M. Peterson, 535 North Dearborn St., Chicago, Secretary.
- Annual Congress on Medical Education and Licensure, Chicago, Feb. 13-14.  
Dr. W. D. Cutter, 535 North Dearborn St., Chicago, Secretary.
- Eastern Section, American Laryngological, Rhinological and Otological Society, Boston, Jan. 11. Dr. Frank E. Kittredge, Masonic Temple, Nashua, N. H., Chairman.
- Middle Section, American Laryngological, Rhinological and Otological Society, Sioux City, Iowa, Jan. 19-20. T. R. Gittins, Davidson Bldg., Sioux City, Iowa, Chairman.
- Southern Section, American Laryngological, Rhinological and Otological Society, New Orleans, Jan. 14. Dr. Francis E. LeJeune, Maison Blanche, New Orleans, Chairman.
- Western Section, American Laryngological, Rhinological and Otological Society, Spokane, Wash., Jan. 29. Dr. Frederic G. Sprowl, Medical Arts Bldg., Spokane, Wash., Chairman.

# Current Medical Literature

## AMERICAN

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Titles marked with an asterisk (\*) are abstracted below.

### American Heart Journal, St. Louis

16: 387-514 (Oct.) 1938

Infarction of Lateral Wall of Left Ventricle: Electrocardiographic Characteristics. F. C. Wood, C. C. Wolferth and S. Bellet, Philadelphia.—p. 387.

\*The Heart in Pneumoconiosis. C. B. Coggin, D. E. Griggs and W. L. Stilson, Los Angeles.—p. 411.

The Social Component in Heart Disease. Ethel Cohen, Boston.—p. 422.

Study of Chest Leads of Electrocardiogram with an Evaluation of Positions of Precordial Electrode. J. C. Edwards and J. B. Vander Veer, Philadelphia.—p. 431.

Cardiac Output in Compensation and Decompensation in the Same Individual. J. McGuire, Rose Shore, V. Hauenstein and F. Goldman, Cincinnati.—p. 449.

Effects of Intravenous Administration of Digitalis Bodies on Patients with Transient Ventricular Fibrillation. S. P. Schwartz and A. Jezer, New York.—p. 462.

Factors of Error in Blood Pressure Readings: Survey of Methods of Teaching and Interpretation. I. S. Wright, R. F. Schneider and H. E. Ungerleider, New York.—p. 469.

Effect of Valvular Heart Disease on Dynamics of Circulation: Observations Before, During and After Occurrence of Heart Failure. H. J. Stewart, J. E. Deitrick, R. F. Watson, C. H. Wheeler and N. F. Crane, New York.—p. 477.

**Heart in Pneumoconiosis.**—Coggin and his co-workers ascertained the incidence of pulmonary cardiac disease in 205 cases of pneumoconiosis, its frequency as a cause of congestive failure and whether the cardiac changes could be detected clinically and roentgenologically. Of these cases 102 occurred in the 19,800 necropsies performed at the Los Angeles County Hospital in the last twenty years, and in the remaining 103 cases there was an adequate history of exposure to silica, and roentgenograms showed the characteristic pulmonary changes of pneumoconiosis. Hypertrophy of the right ventricle was present in 44.1 per cent of the 102 cases that were studied post mortem. If hypertrophy of both ventricles is included, right ventricular hypertrophy occurred in 58.8 per cent of the cases. Definite congestive cardiac failure was found more frequently in these cases (51 per cent) than was tuberculosis (40.2 per cent). It was usually a terminal event. Therefore when it occurs clinically the prognosis is grave. If pneumoconiosis is uncomplicated by tuberculosis or other pulmonary infection, death from cardiac failure is to be expected. The clinical diagnosis of cor pulmonale in pneumoconiosis is suggested by accentuation of the pulmonic second sound, marked cyanosis, right axis deviation in the electrocardiogram and characteristic changes in the postero-anterior roentgenogram; that is, prominence of the pulmonary conus, elevation of the cardiac apex and an increase of the broad or basal diameter in the absence of enlargement of other diameters.

16: 515-642 (Nov.) 1938

Dynamics of Hypertension. C. J. Wiggers, Cleveland.—p. 515.

Treatment of Angina Pectoris by Methods Which Appear to Promote More Adequate Filling of the Heart: Presidential Address. W. J. Kerr, San Francisco.—p. 544.

Vascularization of Atherosclerotic Lesions. T. Leary, Boston.—p. 549.

Use of Metrazol in Complete Heart Block with Adams-Stokes Syndrome: Report of Four Cases. H. C. Lueth, Evanston, Ill.—p. 555.

\*Use of Quinidine in Treatment of Arrhythmias and Tachycardias Caused by Digitalis Intoxication: Note on Possibility of "Spontaneous Redigitalization" Following Rapid Diuresis. B. A. Gouley and L. Soloff, Philadelphia.—p. 561.

Acute Nephritis with Cardiac Failure: Report of Two Cases. A. E. Feller, Iowa City, and H. M. Hurevitz, Davenport, Iowa.—p. 568.

New Sensitive Recording Oscilloscope. I. Friedman, L. H. Ott and A. W. Oughterson, New Haven, Conn.—p. 575.

**Quinidine in Digitalis Arrhythmias.**—Digitalis, under certain conditions, may accelerate cardiac failure in a manner so insidious that the undesirable effect may be overlooked entirely. The electrocardiographic changes may be the first

to show evidence of poisoning and the most reliable guides to the use of the drug. Gouley and Soloff report two cases in which serious digitalis poisoning manifested itself by cardiac arrhythmias, nodal and ventricular tachycardia and auriculo-ventricular dissociation. These disturbances continued despite withdrawal of the drug. Quinidine therapy was useful in restoring normal rhythm in one case but was of no avail in the other. Its failure in this case was believed to be due to inadequate dosage and to the state of advanced cardiac decompensation. Another factor, however, was a cumulative effect of digitalis, possibly caused by a mobilization of the drug in the circulation during diuresis.

### American J. Digestive Diseases, Huntington, Ind.

5: 549-656 (Nov.) 1938

Early Cancer of Stomach and Its Clinical Significance. W. C. MacCarty Sr., Rochester, Minn.—p. 549.

III. Diagnosis of Colitis Associated with Virus of Lymphogranuloma Venereum by Bowel Antigen. M. Paulson, with technical assistance of Betty Kravetz, Baltimore.—p. 554.

\*Bacillary Dysentery: Late Results and Relationship to Chronic Ulcerative Colitis. P. W. Brown and J. A. Bagen, Rochester, Minn.—p. 562.

Studies of Adenomatous Polyps and Carcinoma of the Colon. P. Klemperer, New York.—p. 566.

Study of Gallbladder Function. H. Necheles, Chicago.—p. 568.

The Problem of Gallbladder Infection. M. E. Rehfuess and G. M. Nelson, Philadelphia.—p. 571.

Relationship of Lesions of Cystic Duct to Gallbladder Disease. W. H. Cole and L. J. Rossiter, Chicago.—p. 576.

Endocrines in Relation to Gastrointestinal Tract. J. B. Collip, Montreal.—p. 587.

\*Treatment of Hemorrhagic Tendency in Jaundice, with Special Reference to Vitamin K. A. M. Snell, H. R. Butt and A. E. Osterberg, Rochester, Minn.—p. 590.

Value of Combined Study of Newer Laboratory Test in Differential Diagnosis of Toxic and Obstructive Jaundice Including Blood Phosphatase, Cholesterol Partition, Galactose Tolerance and Glucose Tolerance. H. Shay and P. Fieman, Philadelphia.—p. 597.

Proved Case of Recovery from Fatty Metamorphosis of Liver After Treatment with Lipocain. D. H. Rosenberg, Chicago.—p. 607.

Effect of Therapeutic Agents on Volume and Constituents of Bile. C. R. Schmidt, J. M. Beazell, A. J. Atkinson and A. C. Ivy, Chicago.—p. 613.

A Modern Conception of Gastric Secretory Functions, Based on Recent Investigations and Newer Interpretations. S. Morrison, Baltimore.—p. 617.

**Relation of Bacillary Dysentery to Colitis.**—Brown and Bagen discuss the late results of 140 cases of bacillary dysentery, studied previously by Kinsella, more than sixteen years since the epidemic. Fifteen patients died during the epidemic. Twenty-three patients could not be traced but they apparently were well when they were dismissed. Twenty-four patients died months or years after their dismissal. These patients also apparently were well and had no intestinal symptoms traceable to the epidemic. The stools of forty-five patients yielded *Shigella paradysenteriae*. Seventy-seven patients are known to have lived for from one to seventeen years and did not have any intestinal symptoms after their dismissal. A form of chronic ulcerative colitis developed in only one of the patients. The incidence of intestinal ulceration of a chronic type following large epidemics of dysentery during wars is exceedingly small. Intensive cultural and serologic investigations of the lesions of typical chronic thrombo-ulcerative colitis for organisms of the *Shigella* variety have yielded largely negative results. The results of serologic studies in cases of regional enteritis have been inconclusive so far. Sufficient evidence is not at hand to consider the *Shigella* group of organisms as the cause of chronic thrombo-ulcerative colitis. If chronic ulcerative disease of the intestine develops only in one of every 100 cases of acute dysentery, the suffering in that one case warrants every possible effort to stamp out dysentery.

**Vitamin K in Hemorrhagic Tendency in Jaundice.**—Snell and his co-workers administered to more than thirty patients, most of whom had obstructive jaundice, from 200 to 1,000 mg. of concentrates containing vitamin K prepared from putrefied fish meal, together with bile salts or human bile obtained from a biliary fistula. The bile or bile salts were mixed with cold pineapple juice and given by mouth in doses of from 75 to 150 cc. before each meal. A typical response of both prothrombin time and the concentration of prothrombin to vitamin K and bile when administered together has been

obtained repeatedly. The prothrombin time decreased to within normal limits within a period of from twenty-four to seventy-two hours and the prothrombin itself showed a quantitative increase. Active bleeding has at the same time been controlled in several instances. It appears that the vitamin alone will not accomplish this result if bile is excluded from the intestine, while bile or bile salts have some definite effect, presumably because these substances facilitate absorption of the vitamin which is already present in the intestinal tract. In the presence of injury of the liver larger amounts of vitamin K are required to achieve the desired effect. Presumably the chemical laws governing mass action are operative in this connection. This treatment offers considerable hope for the ultimate control of the hemorrhagic diathesis in jaundiced persons.

### American Journal of Ophthalmology, St. Louis

21:1203-1314 (Nov.) 1938

- Inclusion Blepharitis: Study of Pathologic Changes in the Conjunctiva and Cervix. A. E. Braley, Iowa City.—p. 1203.  
Treatment of Experimentally Produced Exophthalmos with Thyroxine and Other Iodine Compounds. G. K. Smelser, New York.—p. 1208.  
Lectures on Motor Anomalies: III. Signs and Symptoms of Heterophoria. A. Bielschowsky, Hanover, N. H.—p. 1219.  
Studies on Inclusion Blepharitis: III. Experimental Considerations of Etiology. L. A. Julianelle, R. W. Harrison and A. C. Lange, St. Louis.—p. 1230.  
The Histopathology of Papilledema. B. Samuels, New York.—p. 1242.  
Value of Muscle-Balance Tests in Routine Refraction. J. E. Lebensohn, Chicago.—p. 1259.

### Archives of Internal Medicine, Chicago

62:723-902 (Nov.) 1938

- Changes in the Liver Produced by Chronic Passive Congestion, with Special Reference to the Problem of Cardiac Cirrhosis. E. W. Boland, Los Angeles, and F. A. Willius, Rochester, Minn.—p. 723.  
Enlargement of Liver in Diabetic Children: I. Its Incidence, Etiology and Nature. A. Marble, Priscilla White, Isabel K. Bogan and Rachel M. Smith, Boston.—p. 740.  
Id.: II. Effect of Raw Pancreas, Betaine Hydrochloride and Protamine Insulin. Priscilla White, A. Marble, Isabel K. Bogan and Rachel M. Smith, Boston.—p. 751.  
\*Study of Deranged Carbohydrate Metabolism in Chronic Infectious Hepatitis. J. W. Conn, L. H. Newburgh, Margaret W. Johnston and J. M. Sheldon, Ann Arbor, Mich.—p. 765.  
Specificity of Agglutinin Reaction for Shigella Dysenteriae: I. Agglutination Reaction in Chronic Bacillary Dysentery: Serologic and Bacteriologic Study of Forty-Seven Cases. T. T. Mackie, with assistance of Mildred Schweiger and Mary S. B. Gaillard, New York.—p. 783.  
Relation of Age to Renal Pressor Substance. E. B. Grossman and J. R. Williams Jr., Nashville, Tenn.—p. 799.  
Relation of Renal Pressor Substance to Hypertension of Hydronephrotic Rats. J. R. Williams Jr., R. Wegria and T. R. Harrison, Nashville, Tenn.—p. 805.  
\*Fatal Anaphylactic Shock in Man. J. Ziskind and H. J. Schattenberg, New Orleans.—p. 813.  
\*Coronary Occlusion With and Without Pain: Analysis of 100 Cases in Which Autopsy Was Done with Reference to Tension Factor in Cardiac Pain. L. W. Gorham and S. J. Martin, Albany, N. Y.—p. 821.  
Cardiac Pain: Experimental Study with Reference to Tension Factor. S. J. Martin and L. W. Gorham, Albany, N. Y.—p. 840.  
Coccidioides Infection (Coccidioidomycosis): II. Primary Type of Infection. E. C. Dickson, San Francisco, and Myrnie A. Gifford, Bakersfield, Calif.—p. 853.  
Pulsating Angioma (Generalized Telangiectasia) of Skin Associated with Hepatic Disease. D. H. Williams and A. M. Snell, Rochester, Minn.—p. 872.  
Review of Neuropsychiatry for 1938. S. Cobb, Boston.—p. 883.

**Carbohydrate Metabolism in Hepatitis.**—Conn and his colleagues studied the nature of the disturbed carbohydrate metabolism associated with chronic ascending infectious hepatitis in six cases. All exhibited periods of spontaneous hypoglycemia. The glycemic response to ingested dextrose was grossly abnormal. A short period of fast or of carbohydrate restriction resulted invariably in severe hypoglycemia. Data obtained by indirect calorimetry indicated normal oxidation of dextrose under a variety of conditions. Besides the disturbance in carbohydrate metabolism, microscopic examination of biopsy or necropsy material showed chronic cholecystitis and ascending infectious hepatitis leading to early biliary cirrhosis. The authors believe that this disturbance in carbohydrate metabolism, although common, is frequently unrecognized or interpreted wrongly. In the early stage the glycogenic function of the liver appears to be seriously impaired. Since in their cases a hyperglycemic response occurred after ingestion of dextrose and since dextrose was oxidized at the normal

rate under the same conditions, the excess dextrose in the blood stream must be explained by impaired glycogenesis. They believe that this impairment in glycogenesis is one of rate rather than one of total disability, since the blood sugar returns to the fasting level in from four to five hours after ingestion of dextrose and since removal of dextrose is not explained by increased oxidation. The slow rate of glycogenesis accounts for the prolonged hyperglycemia. This delayed removal from the blood stream of absorbed carbohydrate results in postprandial hyperglycemia and glycosuria. Recovery of the glycogenic function appears to parallel the disappearance of the active infection. With the involvement of the glycogenolytic function of the liver, periods of hypoglycemia become manifest. This may be easily mistaken for hyperinsulinism. Respiratory data obtained during the hypoglycemic phase of this disturbance indicate that the low blood sugar levels are not the result of overoxidation of dextrose, as is the case in true hyperinsulinism. Hyperglycemia and glycosuria simulating diabetes mellitus may be a manifestation of one phase of hepatic dysfunction, and periodic spontaneous hypoglycemia may be the manifestation of further hepatic injury in the same patient at different times in the course of hepatitis. This suggests that the hypothetical conception of "dysinsulinism" is probably not the true underlying physiologic mechanism involved in many cases. Since oxidation of dextrose is normal in both the hyperglycemic and the hypoglycemic phases, it appears that hypo-insulinism alternating with hyperinsulinism is not the explanation. Hepatogenic hypoglycemia seems a more likely explanation. Even though the anatomic changes in the liver may be slight, the presence of chronic biliary infection may lead to functional disturbances in the metabolism of carbohydrate. A short period of fast or sharp restriction of the intake of carbohydrate gave rise in the authors' patients to extremely low blood sugar levels. It appears that this response to carbohydrate restriction is a sensitive test of the ability of the liver to deal normally with carbohydrate. Patients who suffer from periodic spontaneous hypoglycemia or whose dextrose tolerance curves are suggestive of diabetes in association with a low blood sugar level during fasting should be investigated for the presence of infection of the biliary tract. The condition may be greatly helped or even alleviated to the stage of clinical cure if the diagnosis of infectious hepatitis is made early and if appropriate surgical treatment is instituted.

**Fatal Anaphylactic Shock in Man.**—Ziskind and Schattenberg report a case of fatal anaphylactic shock following the second intravenous injection of a foreign protein. At necropsy the gross pathologic changes were congestion of the liver and more moderate congestion of the other organs. General enlargement of the lymph nodes and a persistent thymus gland were also noted. The significant microscopic changes were dilatation and congestion of the hepatic sinusoids and the alveolar capillaries of the lungs. There was an apparent relative increase in the leukocytes and the eosinophils within these vessels. The alveoli were compressed in some areas and dilated in others, and in some instances their walls were ruptured. The malpighian corpuscles of the spleen were increased in size and had large germinal centers. It is suggested that the mechanism of death of this patient was capillary dilatation, especially of the liver, with a corresponding fall in blood pressure and cardiac failure.

**Coronary Occlusion With and Without Pain.**—In a study of the clinical histories and necropsy data for 100 patients with proved coronary occlusion, Gorham and Martin found that forty-two patients had no cardiac pain, indicating a higher frequency of painless occlusion than is generally recognized. The fifty-eight patients who suffered from cardiac pain in a fatal attack tended to be younger. The peak mortality was ten years earlier in men than in women. A history of preceding attacks of anginal pain and of hypertension was more common, pain overshadowed dyspnea as a symptom and a pericardial friction rub was heard much more often. Actual thrombosis, acute infarction, acute pericarditis and milder grades of coronary sclerosis were encountered more frequently in this group of fifty-eight patients. The location of the infarct

and the rupture of the ventricle, with resulting hemopericardium, bore no relation to pain. The forty-two patients who had no pain in a fatal attack of coronary occlusion tended to be older than those who had pain, the peak mortality was a decade earlier in men, a history of preceding attacks of anginal pain and of hypertension was less common, dyspnea was generally a prominent symptom and a pericardial friction rub was rarely heard. Old infarcts, with absence of actual thrombosis and pericarditis, were more frequent. Sclerosis of the coronary arteries was slightly though not significantly encountered more often. The location of the infarct and the rupture of the ventricular wall, with resulting hemopericardium, bore no direct relation to the absence of pain. The authors have reexamined the old mechanical theory of cardiac pain advocated by Allbutt and Wenckebach and more recently by Herrmann, which has been generally discarded in favor of Lewis's theory of ischemia in the light of their study, and the role of a tension factor has been emphasized. The tension factor seems to offer a reasonable explanation not only for the presence but for the absence of pain in cases of coronary occlusion. Added support for the importance of the factor of tension in the production of cardiac pain has been obtained by an experimental study on animals.

### Archives of Physical Therapy, Chicago

19: 593-656 (Oct.) 1938

- Contributions of Physical Therapy to Medicine. F. H. Krusen, Rochester, Minn.—p. 597.  
Clinical Aspects of Reaction of Degeneration. J. F. Bateman, Columbus, Ohio, and B. Billman, Cincinnati.—p. 603.  
Treatment of Painful Bursae of the Shoulder. A. A. Martucci, Philadelphia.—p. 611.  
Fever Therapy in Ocular Diseases. J. M. Berris and M. K. Newman, Detroit.—p. 615.  
Sterility of Male Animals Induced by Radiant Heat. U. Giles, A. L. Harvey and F. W. Dampere, New Orleans.—p. 619.  
Physical Therapy and Occupational Therapy in Fractures. H. E. Mock, Chicago.—p. 625.  
Low Voltage Wave Current in Vascular Therapy. E. Bettmann, New York.—p. 633

### California and Western Medicine, San Francisco

49: 353-424 (Nov.) 1938

- Induction of Labor: Some Difficulties. W. B. Thompson, Los Angeles.—p. 358.  
Estrogenic Hormones: Their Clinical Usage. C. F. Fluhmann, San Francisco.—p. 362.  
Muscle Grafts: In the Surgery of the Heart and Lungs. H. B. Stephens and H. Benteen, San Francisco.—p. 366.  
\*Geriatrics: Contribution of Twenty-Five Carefully Studied Patients Who Are Active and in Good Health Beyond Eighty Years of Age. L. J. Brunie, Pasadena.—p. 369.  
Health Protection and Care for the Less Than Two Thousand Dollar Group. N. G. Hale, Sacramento.—p. 372.  
Value of Diet Analysis in Pediatric Practice. Rieta C. Hough and M. J. Walsh, San Diego.—p. 374.

**Longevity.**—Brunie chose for study thirteen men and twelve women active and in good health in the ninth decade of life. The study includes careful medical, dietary and social history, physical examination, blood count, urinalysis, an electrocardiogram and a fluoroscopic examination of the chest. By "active and in good health" he means that these persons were driving their own automobiles, some were still working for a livelihood and many were active in play—trap shooting, going to the races and theater, and even dancing and golf. Most of them took genuine interest in a variety of hobbies. Mentally they were all active and alert. Heredity, without question, is the fundamental requirement for longevity. In the present series there was only one person who did not have immediate relatives—that is, parents or grandparents, brothers or sisters—who had lived or were living beyond 75 years. The incidence of infection in their lives was relatively unimportant. Most of them had had the usual childhood diseases. Three had pneumonia in adult life and four had influenza at the time of the 1918 epidemic. Four gave histories of tonsillitis. One third of the group gave histories of migraine headaches occurring in earlier life, although none of them complained of more than occasional mild headaches at the present time. An interesting endocrine factor is that 60 per cent of the men had retained their sexual powers to an average age of 80 years. This would indicate that their general endocrine systems were

still functioning. There was no case of syphilis and only one mild case of tuberculosis. One person, a man, recovered from pneumonia at the age of 91 years. Study revealed that moderation rather than abstinence was the rule for these people. Obesity shortens life, and none of these people were overweight. True arteriosclerosis was not present in any of the subjects.

### Canadian Public Health Journal, Toronto

29: 477-526 (Oct.) 1938

- The Present Problem in Infant Mortality. L. A. Pequegnat, Toronto.—p. 477.  
Demonstration of Types of Bacillus Typhosus by Means of Preparations of Type II Vi Phage: II. Stability and Epidemiologic Significance of V Form Types of Bacillus Typhosus. J. Craigie and Chun Hui Yen, Toronto.—p. 484.  
Diphtheria Immunization, with Special Reference to Local Campaign. L. M. Morton, Yarmouth, N. S.—p. 497.  
Seasonal Variation in Response of Guinea Pigs to Toxoid. G. D. W. Cameron, Toronto.—p. 500.  
The Public Health Nurse in Venereal Disease Control. Margaret Norton, Brantford, Ont.—p. 504.  
Some Industrial Skin Lesions. H. L. Scammell, Halifax, N. S.—p. 508.

### Delaware State Medical Journal, Wilmington

10: 223-238 (Nov.) 1938

- Exophthalmic Goiter: Its Medical Treatment: End Results in 2,600 Cases. I. Bram, Philadelphia.—p. 223.  
Trichiniasis: Report of Five Cases. E. R. Miller, Wilmington.—p. 229.  
To the Nurses. D. J. Layton, Georgetown.—p. 233.

### Iowa State Medical Society Journal, Des Moines

28: 525-598 (Nov.) 1938

- Management of Skull Fractures and Cerebral Injuries. H. E. Mock, Chicago.—p. 525.  
Recent Advances in Chest Surgery. N. B. Anderson, Des Moines.—p. 536.  
Study of Meningeal Permeability, with Special Regard to Influence of Sterile Meningitis on Permeability Quotients of Schizophrenics. S. L. Sands, Iowa City.—p. 539.  
Treatment of Convergent Squint in Private Practice. J. A. Thorson, Dubuque.—p. 547.  
Retrolbulbar Neuritis of Uncertain Origin. E. C. Nowak, New Hampton.—p. 551.  
\*Sublethal Pulmonary Emboli. D. H. Kaump and V. C. Robinson, Des Moines.—p. 554.

**Sublethal Pulmonary Emboli.**—From a study of five cases it is apparent to Kaump and Robinson that the picture in sublethal embolus is exactly that presented by a lethal embolus except for the lesser gravity of the symptoms. The predominant symptoms in sublethal embolus included anxiety of the patient, cough with bloody sputum in one instance, cyanosis, dyspnea, rapid pulse and chest pain. The diagnosis of sublethal embolus must be suspected in the presence of any or all of these symptoms. Occasionally a patient is seen who has only a slight dyspnea, slight chest pain and minor evidences of shock. In the differential diagnosis, coronary thrombosis and pulmonary arteriolar sclerosis must be considered. The predisposing factors in the patients with sublethal embolus include previous heart disease, four out of five, and obesity, three out of five. Next to the prevention of embolus formation the second most important factor is the recognition of sublethal embolus when it does occur. If the symptoms of sublethal embolus were recognized more frequently, simple prolonged rest might prove valuable in the prevention of the second and often fatal embolic attack.

### Journal of Immunology, Baltimore

35: 329-414 (Nov.) 1938

- Concentration of Tetanic Antitoxin by Adsorption. D. von Klobusitzky, São Paulo, Brazil.—p. 329.  
Influence of Alarm Reaction on Development of Anaphylactic Shock. S. Karady, H. Selye and J. S. L. Browne, Montreal.—p. 335.  
Antigenic Structure of Shigella Alkalescens (Andrewes) and Demonstration of Antibodies in Serum of Patients with Shigella Alkalescens Infections. E. Neter, Buffalo.—p. 339.  
Photodynamic Action of Methylene Blue on Antipneumococcus Serum. V. Ross, New York.—p. 351.  
Photodynamic Action of Methylene Blue on Diphtheric Antitoxin. V. Ross, New York.—p. 371.  
Character of Dissociative Changes in Escherichia Coli Affecting Immunizing Values. J. C. Torrey, New York.—p. 379.  
Antigenic Qualities of Antitoxins. A. J. Weil, I. A. Parfentjev, Pearl River, N. Y., and K. L. Bowman, Brooklyn.—p. 399.



**Journal of Infectious Diseases, Chicago**

63: 129-224 (Sept.-Oct.) 1938

- Small Colony Variation in *Bacillus Paratyphosus B* (Tidy) and Other Bacteria, with Special Reference to the G Type of Hadley. A. Hadley, Edinburgh, Scotland.—p. 129.
- Demonstration of Plasma Anticoagulant in Exudates of Bacterial Origin. E. Neter, Buffalo.—p. 193.
- Studies in Metabolism of *Coccidioides Immitis* (Stiles). R. A. Stewart and K. F. Meyer, San Francisco.—p. 196.
- Response of Specifically Immunized Mice to Reinoculation with Virus of St. Louis Encephalitis, with Especial Attention to the Development of Myelitic Symptoms. Enid A. Cook, Chicago.—p. 206.
- Effect of Splenectomy and Blockade on Protective Titer of Antiserum Against *Trypanosoma Equiperdum*. L. R. Kuhn, Chicago.—p. 217.

**Journal of Nutrition, Philadelphia**

16: 407-510 (Nov.) 1938

- Ascorbic Acid Content of Chick Blood. A. D. Holmes and F. Tripp, Boston, and G. H. Satterfield, Raleigh, N. C.—p. 407.
- Does Fat in the Diet Affect the Thyroid? R. E. Remington, Charleston, S. C.—p. 417.
- \*Availability of Iron in Various Foods. Leah Ascham, Mary Speirs and Dorothy Maddox, Experiment, Ga.—p. 425.
- Quantitative Study, by Means of Spectrographic Analysis, of Copper in Nutrition. Florence I. Scouler, Iowa City.—p. 437.
- Histopathology of Neuromalacia and "Curled Toe" Paralysis in the Chick Fed Low Riboflavin Diets. P. H. Phillips and R. W. Engel, Madison, Wis.—p. 451.
- Toxicity of *Aspergillus Sydowi* and Its Correction. D. W. Woolley, J. Berger, W. H. Peterson and H. Steenbock, Madison, Wis.—p. 465.
- Effect of Exercise and Chills on Heat Loss from the Nude Body. J. D. Hardy, Ade T. Milhorat and E. F. Du Bois, with technical assistance of G. F. Soderstrom, New York.—p. 477.
- Heat Loss from the Nude Body and Peripheral Blood Flow at Temperatures of 22 to 35 C. J. D. Hardy and G. F. Soderstrom, New York.—p. 493.

**Availability of Iron in Foods.**—Ascham and her collaborators determined the hematopoietic value of certain leafy vegetables which are important sources of iron in southern diets. They found that a greater hemoglobin gain was obtained with the canned leaves plus the cooking liquid of turnip greens and collards than with the dried forms of these greens. The iron of the canned turnip green leaves was less available than that of the dried greens. The foods studied fall into the following descending order in respect to the availability of their iron for the regeneration of hemoglobin: black-eyed peas and spinach, turnip greens and kale, collards and mustard, head lettuce and, finally, tender-green and leaf lettuce. In these foods the ionizable iron and the iron available for hemoglobin synthesis were not identical.

**Journal of Pediatrics, St. Louis**

13: 619-804 (Nov.) 1938

- Inspissation of Secretion, Dilatation of Ducts and Acini, Atrophy and Fibrosis of Pancreas in Infants: Clinical Note. K. D. Blackfan and C. D. May, Boston.—p. 627.
- Carotinoids and Vitamin A of the Blood. S. W. Clausen and A. B. McCoord, Rochester, N. Y.—p. 635.
- \*Experimental Therapy of Acute Leukemia with Extracts of Bone Marrow. J. V. Cooke, St. Louis.—p. 651.
- Importance of Deficit of Sodium and Chloride in Dehydration. D. C. Darrow, New Haven, Conn.—p. 670.
- Accomplishments in Maternal and Child Health and Crippled Children Services Under the Social Security Act. Martha M. Eliot, Jessie M. Bierman and A. L. Van Horn, Washington, D. C.—p. 678.
- Further Observations on Metabolism and Clinical Uses of Sodium Lactate. A. F. Hartmann, Anne M. Perley, J. Basman, Martha V. Nelson and Cécile Asher, with technical assistance of Marie Morton, St. Louis.—p. 692.
- Acute Epidemic Encephalitis in St. Louis. T. C. Hempelmann, St. Louis.—p. 724.
- Effect of Vitamin D on Linear Growth in Infancy: II. Effect of Intakes Above 1,800 U. S. P. Units Daily. P. C. Jeans and Genevieve Stearns, Iowa City.—p. 730.
- Encephalitis Rumatica (Chorea Minor of Sydenham): Its Diagnosis and Course. H. McCulloch, St. Louis.—p. 741.
- Irregular Extensions of End of Shaft in X-Ray Photograph in Congenital Syphilis, with Pertinent Observations. E. A. Park and Deborah A. Jackson, Baltimore.—p. 748.
- Remarks on Case of Congenital Idiopathic Hypertrophy of the Heart. G. F. Powers and P. M. LeCompte, New Haven, Conn.—p. 760.
- \*Diabetes and Pregnancy: Observations on Offspring with Pathologic Report. E. S. Smyth and Mary B. Olney, San Francisco.—p. 772.
- Congenital Hypertrophic Pyloric Stenosis, with Special Reference to Surgical Treatment. K. H. Tallerman, London, England.—p. 787.
- Systematic Health Work for Mother and Child. K. Utheim-Toverud, Oslo, Norway.—p. 796.

**Acute Leukemia and Extracts of Bone Marrow.**—Cooke tested the validity of a new hypothesis as to the nature of leukemia. The hypothesis assumes that acute leukemia is due to an acquired defect in normal marrow function charac-

terized by the inactivation or destruction of one of the normal factors in hematopoiesis. After making a few observations with the use of extracts of liver, spleen and thymus, without apparent effect, the action of extracts of fresh red bone marrow on acute leukemia was studied. A study of the patients with acute leukemia treated with bone marrow extracts shows two with complete remission of two and four months, two with similar complete remissions for shorter periods, two with marked increase in maturation of granular leukocytes, four in whom the disease remained clinically arrested or quiescent for from three to six months, two in whom rather prompt decrease in the size of leukemic enlargements of the lymph nodes and spleen was observed after the treatment was given and other patients in whom neither the clinical course nor the leukemic blood picture was affected. That the bone marrow extract employed was responsible for any or all the favorable changes observed is without proof. All patients received transfusions at intervals and other symptomatic treatment. It is true, however, that of fifty patients with acute leukemia from the same clinic and under observation during the ten years preceding these experiments, who were also given frequent transfusions, none showed a remission or any increase in the granular leukocytes to the degree observed in certain of the present patients. The evidence furnished by the observations is inconclusive, but the improvement in at least six cases did not appear to be merely coincidental. However, if the changes observed were related to the replacement of some deficiency in a physiologic mechanism the stimulation was inadequate and incomplete, since even those patients with remissions relapsed and later injections were relatively impotent. The author believes that a definite effect on the disease was produced but that it was only partial and imperfect, as though only one of possibly several necessary substances was being supplied and that only sufficient to modify the progress of the disease.

**Diabetes and Pregnancy.**—Smyth and Olney state that since 1922 nineteen infants have been born of women whose pregnancy was considered complicated by diabetes. In fourteen of the mothers glycosuria appeared only with gestation and was controlled by diet or by diet and temporary use of insulin, which suggests glycosuria from causes other than diabetes mellitus. Of the entire group, eleven gave birth to excessively large infants. The infant's blood sugar, even allowing for the effect of predelivery insulin, may be low. The cord blood sugar may anticipate this finding by showing a much lower level than that of the maternal blood taken simultaneously. In two of the infants projectile vomiting and cyanosis were striking features, quite possibly related to persistent hypoglycemia. This interpretation circumvented pyloroplasty, which was suggested for one of the infants. The use of subcutaneous dextrose appeared extremely valuable in carrying the infants through a critical period, after which an apparent adjustment was made. A follow-up of one patient showed a hyperinsulin-like sugar curve at 4 years of age. Reports of postmortem studies of infants born of diabetic mothers vary. In some no hyperplasia of islet tissue has been found, and the hypoglycemia must be considered functional in type. In others the finding of hypertrophy and hyperplasia of the islets of Langerhans makes the correlation obvious. The relative macrosomia, advanced bone age and more mature genital tract suggest a pituitary effect. Complete endocrine pathologic study is reported but the interrelationship is best described as dysfunction. Perhaps some interrelationship will be found to account for the mild as well as the fatal hypoglycemia of the newborn infant. Fetal glycogen storage hypertrophy also is postulated as a possible cause for some of the pathologic signs.

**Medical Annals of District of Columbia, Washington**

7: 335-370 (Nov.) 1938

- Study of Cystine and Tryptophan Content of Normal and Pathologic Serums. H. S. Milone and M. X. Sullivan, Washington.—p. 335.
- Chronic Sinusitis in Children, with Special Reference to X-Ray Therapy. P. A. McLendon, Washington.—p. 341.
- Value of Combined Measurements of Circulation Time and Venous Pressure in Heart Failure. H. H. Hussey, Washington.—p. 350.
- Chronic Constrictive Pericarditis (Chronic Cardiac Compression): Report of Three Cases Successfully Operated on. W. M. Yater, Washington.—p. 354.

**Medical Bull. of Veterans' Adm., Washington, D. C.**

15: 99-216 (Oct.) 1938

- One Year's Experience with Pharmacologic Shock Therapy of Chronic Schizophrenia. C. N. Baganz.—p. 99.
- Heart Weight and the Measurement of Cardiac Silhouette. J. A. Reisinger and Blanche B. Wilcox.—p. 108.
- Avertin Basal Anesthesia with Ether, Nitrous Oxide Oxygen and Ethylene; from an Observation of 500 Cases. G. A. Resta.—p. 118.
- Ganglionectomy in Vascular Disturbances of Extremities. H. E. Bundy.—p. 121.
- Survey of Results of Operative Intervention in Various Surgical Disorders of Psychotic Patients, with Consideration of Feasibility of Major Collapse Measures in Tuberculous-Psychotic Patients. W. A. Loeb and E. A. Wilcox.—p. 124.
- Standardization of Methods of Diagnosis of Tuberculosis in Psychotic Patients. T. J. Hardgrove.—p. 131.
- Cerebral Accidents. H. Rubin.—p. 135.
- Sakel's Hypoglycemic Insulin Treatment of Psychoses. L. H. King.—p. 141.
- Coexistence of Pulmonary Tuberculosis and Syphilis. W. C. Nalty.—p. 151.
- Nontuberculous Respiratory Diseases. E. J. Kehoe.—p. 155.
- Use of Protamine Insulin. S. E. Walker.—p. 160.
- Disability from Weak Foot. I. H. Russotto.—p. 163.
- Management of Sinusitis. O. N. Nelson.—p. 167.
- Early Diagnosis of Intestinal Tuberculosis. J. C. Herrick.—p. 172.

**Minnesota Medicine, St. Paul**

21: 745-816 (Nov.) 1938

- Influence of Age-Determined Factors on Development of Tuberculosis. A. R. Rich, Baltimore.—p. 745.
- Roentgenography of Pulmonary Tuberculosis: New Method for Group Surveys. H. E. Potter, Chicago.—p. 763.
- The Foot and Ankle: Their Discomforts, Deformities and Disabilities. P. Lewin, Chicago.—p. 769.
- Authentic Biographic Data. M. C. Piper, Rochester.—p. 776.
- Nutrition in Pregnancy. R. J. Moe, Duluth.—p. 779.
- Inflammatory Lesions of Cervix and Vagina. L. W. Barry, St. Paul.—p. 784.
- Obstetric Hemorrhage. R. E. Swanson, Minneapolis.—p. 788.

**Missouri State Medical Assn. Journal, St. Louis**

35: 423-466 (Nov.) 1938

- Puerperal Infection. P. Findley, Omaha.—p. 423.
- Country Obstetrics: Review of 600 Cases. W. J. Shaw, Fayette.—p. 426.
- Tuberculosis Complicating Pregnancy: Treatment: Report of Cases. A. C. Henske, St. Louis.—p. 430.
- Evaluation of Mental Factor in Treatment of Physical Disorders. F. A. Carmichael, Fulton.—p. 436.
- \*The Neurotic Factor in Disease. R. E. Britt, St. Louis.—p. 440.
- Effect of Work on the Heart. D. G. Stine, Columbia.—p. 443.
- Role of Parasympathetic Nervous System in True Enuresis. A. Bleyer, St. Louis.—p. 447.
- Infant Feeding: Some Practical Suggestions. C. B. Summers, Kansas City.—p. 449.

**The Neurotic Factor in Disease.**—Britt reviewed more than 500 cases with psychiatric implications admitted to the Firmin Desloge Hospital between 1933 and 1938. In two thirds of these the problem was essentially that of organic disease of the central nervous system brought about through vascular change, trauma, cerebral tumor or infection. Of the remaining third, approximately 40 per cent presented classic mental conditions recognizable as neuroses and psychoses, whereas the remainder, about 120, were mixtures of physical complaints complicated by the attitudes of the patients influencing to varying degrees the onset and course of the disease. In every instance the patient had been admitted to the hospital primarily for some definite physical condition the signs and symptoms of which were unmistakable. To do justice to the patient the physician must take into consideration not only the laws of laboratory procedure but also the laws which regulate the reaction of man to his environment even though these laws cannot be formulated in mathematical or precise physical terms. The emotional and instinctive life of the patient, the family pattern, economic and social situations, may be essential factors in understanding and treating patients when symptoms may not at first suggest a complex origin. A consideration of these factors makes intelligible such symptoms as persistent headache, insomnia, gastrointestinal disturbances, fainting, palpitation, variations in blood pressure, the frequency of attacks of vertigo, refractive disorders and pelvic and abdominal com-

plaints. These symptoms are understandable oftentimes as expressions of both physical and mental inadequacy which may be symptomatic of some definite physical disease, its so-called psychic component.

**New England Journal of Medicine, Boston**

219: 731-776 (Nov. 10) 1938

- Innocent Gallstones and Harmful Cholecystectomy? D. Cheever, Boston.—p. 731.
- \*Thiocyanate Therapy in Vascular Hypertension. E. Massie, C. B. Ethridge and J. P. O'Hare, Boston.—p. 736.
- Value of Palliative Surgical Therapy in Advanced Carcinoma of Gastrointestinal Tract. C. G. Mixer, Boston.—p. 740.
- Angina Pectoris and Its Relation to Coronary Artery Disease. S. A. Levine, Boston.—p. 743.
- Recurrent Appendicitis. C. A. Lamb, Boston.—p. 746.

**Thiocyanate Therapy in Hypertension.**—Massie and his associates administered sodium thiocyanate, according to the method of Barker, under carefully controlled conditions to fourteen patients suffering from uncomplicated vascular hypertension. Before the administration of sodium thiocyanate was begun, all direct treatment was discontinued and control observations were made for three months. There followed a test period of like duration during which a 5 per cent solution of sodium thiocyanate in syrup of wild cherry was given orally. This interval was followed by another control period of three months during which the syrup alone was administered in comparable dosage; the patient remained unaware that the active medication had been omitted. A definite lowering of the blood pressure occurred during the interval of treatment. Compared with the first control period, the average fall in the systolic pressure ranged from 66 to 21 mm. of mercury and the average fall in the diastolic pressure from 33 to 8 mm. The blood pressure in each case generally rose during the second control period, so that eventually the levels noted in the initial control period were approximated. The principal complaints attributable to hypertension were persistent and troublesome headache, nervousness and mild vertigo. These symptoms either decreased appreciably or disappeared entirely under treatment in twelve cases. Insomnia was markedly relieved, so that sound sleep at night was more readily secured. Unusual activity, excitement and emotional upsets were well borne. Symptoms which had been relieved during thiocyanate therapy gradually returned with all their original severity during the second control period when the drug was surreptitiously omitted. Gradually, the blood pressure rose again. The toxic symptoms observed were occasional episodes of transient weakness and infrequent attacks of mild epigastric distress. In addition, nausea, vomiting and marked weakness occurred in one patient and three attacks of angina pectoris in another. Individualization of dosage is required for each patient, frequent blood cyanate determinations and sufficient intelligence on the part of the patient to permit an awareness of early toxic symptoms. For his own safety the patient must be cautioned regarding the symptoms of asthenia and nausea so that the more serious forms of toxicity may be avoided.

**Northwest Medicine, Seattle**

37: 343-378 (Nov.) 1938

- New Plans for Medical Practice. C. T. Sweeney, Medford, Ore.—p. 346.
- Nutritional Deficiencies Complicating Surgery of Gastrointestinal Tract. D. Metheny, Seattle.—p. 349.
- Renal Tuberculosis. C. D. Donahue, Eugene, Ore.—p. 350.
- Nephrectomy Twenty-Five Years After Ureterosigmoid Anastomosis: Instance of Pneumopyonephrosis. R. Falk and R. S. Smith, Boise, Idaho.—p. 353.
- Metrazol Therapy in Schizophrenia. N. K. Rickles, Seattle.—p. 355.
- Rapid Technic for Tonsillectomy Which Avoids Hemorrhage. R. W. Kullberg, Astoria, Ore.—p. 358.

**Oklahoma State Medical Assn. Journal, McAlester**

31: 367-398 (Nov.) 1938

- Bronchoscopy in Oklahoma. L. C. McHenry, Oklahoma City.—p. 367.
- Observation from the Current Year's Experience with Medical Cases in a Children's Hospital. F. C. Neff, Kansas City, Mo.—p. 370.
- Acute Appendicitis. H. Reed, Oklahoma City.—p. 376.
- Cavernous Sinus Thrombosis: Case Reports. T. G. Wails, Oklahoma City.—p. 378.
- Lateral Sinus Thrombosis. D. L. Mishler, Tulsa.—p. 381.

**Public Health Reports, Washington, D. C.**

53: 1961-1990 (Nov. 4) 1938

Isolation of Actinomyces Bovis from Tonsillar Granules. C. W. Emmons.—p. 1967.

53: 1991-2024 (Nov. 11) 1938

\*Incidence and Future Expectancy of Mental Disease. H. F. Dorn.—p. 1991.

Studies on Mechanism of Experimental Intranasal Infection in Mice. C. Armstrong.—p. 2004.

**Incidence and Expectancy of Mental Disease.**—Dorn points out that it is commonly believed that the proportion of the population suffering from mental disease is increasing. For the country as a whole the number of persons hospitalized for mental disease increased more than 40 per cent from 1926 to 1936. The most common explanation for the apparent increase in the incidence of mental disease is the complexity and strain of metropolitan life. Owing to the fact that there is no sharp line of demarcation between normality and abnormality, it is practically impossible to decide whether or not the relative number of persons with mental disease is increasing. Fundamentally mental disease is a cultural concept and varies from one group to another. In some situations the mentally deranged have become soothsayers, medicine men, prophets or group leaders; in other situations the same persons would be incarcerated. From an analysis of the first admissions to mental hospitals in Massachusetts, New York and Illinois this commonly believed increase is not borne out. The number of first admissions per hundred thousand of population decreased among women under 70 years of age in each state. In Massachusetts the same was true for men. In New York and Illinois commitment rates decreased at the younger ages, but after 45 or 50 years of age an increase occurred. Nevertheless mental diseases constitute an important health problem. Unless there is a decrease in the first admission rates to mental hospitals, from 110,000 to 120,000 of the 2,144,800 infants born during 1936 will eventually be committed to a hospital for mental disease. This number excludes the emotionally unstable and unbalanced persons who should be included in a comprehensive mental hygiene program. Owing to the increasing proportion of the population in the older age groups and the increase in life expectancy, an increase in the number of admissions to mental hospitals is to be expected in the future, since rates of mental disease are highest at the older ages. Assuming that the commitment rates for mental disease for the total United States are no greater in 1960 than they were in New York state from 1929 to 1931 inclusive, it is estimated that about 135,000 persons will be committed annually to a mental hospital for the first time. This is nearly twice the present number of first commitments.

**Puerto Rico J. Pub. Health & Trop. Med., San Juan**

14: 1-90 (Sept.) 1938

Rosets in Rat Leprosy. E. V. Cowdry and A. Ravold, San Juan.—p. 3.

Filariasis in Puerto Rican Soldiers: Survey. A. G. Oliver and J. Oliver, San Juan.—p. 18.

Planorbis Corneus Not an Intermediate Host of Schistosoma Mansoni. W. A. Hoffman, San Juan.—p. 24.

Gallbladder Disease in Puerto Rico. F. G. Irwin and A. R. Oller, San Juan.—p. 28.

Chromoblastomycosis in Puerto Rico. A. L. Carrión, San Juan.—p. 37.

**Southwestern Medicine, El Paso, Texas**

22: 429-468 (Nov.) 1938

What Next in Medicine? L. S. Peters, Albuquerque, N. M.—p. 429.

\*Atherosclerosis, Angina and Allergy. G. Werley, El Paso, Texas.—p. 431.

The Endocrinology of Prostatic Hypertrophy. E. Belt, Los Angeles.—p. 434.

Abdominal Surgery and Wangenstein Suction. J. L. Green and H. H. Varner, El Paso, Texas.—p. 439.

Toxemia of Pregnancy. A. J. DePinto, Phoenix, Ariz.—p. 443.

Lead Absorption and Lead Poisoning: III. J. Rogde, El Paso, Texas.—p. 445.

Extra-Uterine Pregnancy of Twenty-Nine Years' Duration with Incidental Ovarian Carcinoma: Case Report. H. M. Mortimer and F. H. Crail, Las Vegas, N. M.—p. 447.

**Atherosclerosis, Angina and Allergy.**—Werley states that coronary sclerosis is found in from 20 to 30 per cent of all men beyond 40 years of age. Anginal attacks are rare in comparison. Many die of acute coronary obstruction with no history of angina pectoris. Of eighty-seven of his cases of cardiac infarct,

only nineteen previously had definite anginal attacks. White states that a sensitive person, especially one with capacity for vascular spasm, may suffer from angina pectoris with relatively little coronary disease behind it, or in rare cases none at all, while an insensitive person may have an appalling amount of disease or even chronic occlusion of both coronary arteries with no pain whatever. The author believes that this hypersensitive group will often be found to be allergic. However, there may be other reasons for the hypersensitivity of the coronary arteries. Angina and coronary sclerosis go together. The presence of angina is a signal of danger that if heeded and followed by correction, especially of bad eating habits, may actually prolong life and thus be advantageous. There is no reason why the coronaries should be exempt. Allergy manifests itself by spasm of smooth muscle especially in the smaller arteries. There is dilatation of capillaries and exudation. The reaction is most violent in those arteries with the most smooth muscle in their walls. In man, the coronary arteries have a heavier coat of unstriated muscle than any other artery of similar size in the body. So, if the law holds, this should be a favorable site for allergic reaction. The author thinks that this may be one reason why the coronary arteries are more often sclerotic than other arteries of their size in other situations. Periarthritis nodosa shows that allergy may manifest itself in the coronary arteries. In the search for the causes of coronary sclerosis and angina pectoris, suspicion has fallen on many things, especially the hectic life of modern civilization. Generally the chief cause of angina pectoris and coronary sclerosis can be traced to what has gone down the gullet. Other factors are of secondary importance. Regardless of other factors, obesity generally comes from eating too much and especially too much fat, along with which always goes cholesterol, the one important cause of atherosclerosis.

**Wisconsin Medical Journal, Madison**

37: 973-1052 (Nov.) 1938

Pneumoperitoneum: Preliminary Report. E. R. Daniels and P. L. Eisele, Statesan.—p. 989.

Nonspecific Infections of the Urinary Tract. C. R. Marquardt, Milwaukee.—p. 994.

Chronic Nasal Sinus Disease. I. Muskat, Chicago.—p. 997.

Unusual Case of Intestinal Obstruction. W. O. Paulson and L. M. Garrett, Eau Claire.—p. 1001.

\*Low Fat Evaporated Milk in Infant Feeding. A. C. Edwards, Madison.—p. 1004.

Preoperative Treatment. I. Schulz, Milwaukee.—p. 1006.

Polyneuritis: Metabolic Disorder: Diagnosis and Treatment. Mabel G. Masten, Madison.—p. 1009.

**Low Fat Evaporated Milk in Infant Feeding.**—Edwards proposes a modification to the evaporated milk formula in order to overcome the difficulties (vomiting, obesity and allergy) encountered in infant feeding with the use of concentrated evaporated milk in private practice. The new product that he suggests using consists essentially of half skimmed evaporated milk prepared by a Wisconsin condensery. This modified milk may be conveniently used for feeding normal infants by diluting it, as recommended by Marriott and Brennemann in the case of regular evaporated milk, with an equal quantity of water and 2 ounces (60 Gm.) of a soluble carbohydrate (a preparation of dextrin and maltose) added to each quart of mixture. Infants receiving the formula did as well as or better than expected. In all cases the digestion was as described by Brennemann in the case of regular evaporated milk. Infants less than 6 weeks of age tolerated it well after a few days on a slightly greater dilution. Vomiting was exceedingly rare. Practically all otherwise normal infants less than 6 months of age tolerated it well and the majority of them made satisfactory weight increases without, however, becoming obese. In the few in whom a more rapid gain was desired it was necessary only to change to a similar formula made with regular evaporated milk. A few infants were encountered whose nutrition and digestion progressed satisfactorily on regular evaporated milk formulas but who cried considerably and apparently had gastrointestinal allergy with symptoms of abdominal spasm. When these infants were given the proposed formula the majority of them improved. Overnourished infants with eczema seemed to fare better when appropriate local treatment was combined with a reduction in caloric intake including the substitution of modified milk for regular evaporated milk in their formulas.

## FOREIGN

An asterisk (\*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

### British Journal of Dermatology and Syphilis, London

50: 575-636 (Nov.) 1938

Twenty-Five Years of Gold Treatment of Lupus Erythematosus. R. Simons.—p. 575.

\*Description and Study of Area of Atrophic Skin Occurring in Men, with Its Relationship to the Common Type of Diffuse Alopecia of the Scalp. P. C. Robertson.—p. 581.

Did Columbus Discover Syphilis? V. Robinson.—p. 593.

**Atrophic Skin in Men.**—Robertson studied the state of the skin and hair of the legs and scalp of 1,171 men between the ages of 20 and 60 years. He found that in a proportion of adult men there occurs on the legs an area of skin with the following characteristics: 1. It is smooth, shiny and hairless and, on exposure to cold, has no goose-skin appearance. It is whiter than normal skin and looks thin and atrophic. 2. It occurs below the knee on the anterior lateral and posterior aspects of the leg and varies in size in different individuals. 3. Its position and extent on one leg are the same as on the other. 4. In appearance and texture it is similar to the bald skin in diffuse alopecia of the scalp. 5. It does not occur before puberty. 6. With the exception of the scalp, no similar area occurs elsewhere on the body. It was found that the majority of men who are bald on the scalp, 379 of the 1,171 men examined, are bald also on the legs, 408 of the entire group. Experiments on nerve and vascular supply carried out on the atrophic skin of the legs and scalp, when compared with shaved normal skin, showed that there is equal sensibility to touch, heat, cold and pain. The "nocifensor" reaction after injury is the same as in normal skin. The reaction to pricked-in epinephrine 1:1,000 and histamine acid phosphate 1:1,000 is the same as of normal skin. When the condition of the cutaneous atrophy on the legs is considered along with diffuse alopecia of the scalp, it is seen that in both conditions the hair loss and the cutaneous atrophy are bilaterally symmetrical (for the denudation of hair is symmetrically outlined on the two sides of the scalp, as it is also on the two legs) and that when there is baldness of the scalp there is generally baldness of the legs. These observations suggest a common causation; a general change occurring in the body. The nature of this change is suggested by consideration of the factors responsible for the maintenance of cutaneous and hirsute health. These factors are vascular supply, nerve supply and nerve influences and the composition of the blood. It therefore appears probable that the change in the body which is responsible for diffuse alopecia of the scalp and for the areas of the cutaneous atrophy on the legs is an alteration of the balance of endocrine secretion and is dependent on the integrity of the testicles. How this produces the cutaneous atrophy and why the areas affected should be localized on the scalp and legs are questions yet unanswered.

### British Journal of Ophthalmology, London

22: 641-704 (Nov.) 1938

\*Prescribing Light: Important Factor in the Care and Treatment of the Eye. C. E. Ferree and G. Rand.—p. 641.

Aplasia of the Optic Nerves. H. Ridley.—p. 669.

Effect of Section of Posterior Ciliary Arteries in the Rabbit. J. V. V. Nicholls.—p. 672.

**Lighting.**—Ferree and Rand contend that the eye, if it is to remain healthy or to cure itself of any of its ills, congenital or acquired, must first be put into a situation calling only for the healthy exercise of its normal functions. Important factors in this situation are the conditions under which it is ordinarily called on to work, the type of work and its illumination. The latter is the more amenable to variation and control. Radical changes cannot be made in the work itself, although the lighting of the work is possible and the more important angle of attack. Lighting equipment of sufficient range and flexibility has been devised, and a great deal of time has been spent in making it available to the public. Thus a new division of the subject of lighting has been created which belongs in its narrower and more technical aspects to the medical profession and in its broader and more general

aspects to the welfare of the worker. The prescribing of light to meet the requirements of the individual person has become a practical possibility and when properly used it will be of significant service in the care and treatment of the eye. The need for it is acute in many of the cases which come under the physician's care.

### Lancet, London

2: 983-1040 (Oct. 29) 1938

\*Further Observations on Hormone Treatment of Imperfect Descent of Testis. A. W. Spence and E. F. Scowen.—p. 983.

Classification of Chronic Nephritis. J. B. Duguid.—p. 987.

\*Chemotherapy in Measles and Whooping Cough: Prophylaxis and Treatment of Complications. A. R. Thompson and C. R. M. Greenfield.—p. 991.

Sulfanilamide in Treatment of Trachoma. R. Kirk, A. R. McKelvie and H. A. Hussein.—p. 994.

Hippuric Acid Synthesis in Schizophrenia. R. Ström-Olsen, G. D. Greville and R. W. Lennon.—p. 995.

**Endocrine Treatment of Imperfect Descent of the Testis.**—Spence and Scowen used gonadotropic substance in the treatment of sixty-five patients with undescended testes. Their conclusions are that treatment of retained testes with gonadotropic extract should be employed in those patients in whom retention does not appear to be due to an anatomic abnormality. The dose in most patients should not be less than 500 rat units intramuscularly twice a week. This treatment should not be employed in patients less than 10 years of age for fear of inducing a precocious puberty. The optimal age for treatment is between 10 and 14. All cases of retractile testes will respond to endocrine therapy within three months. Treatment, however, is unnecessary as they will descend spontaneously before or at puberty. Testes which are situated in the inguinal canal and are movable but cannot be manipulated into the scrotum will probably respond to endocrine therapy (76 in the bilateral and 64 per cent in the unilateral group). A successful result is unlikely if the retained testes are impalpable or are not freely movable. In cases of retained testes which will respond, a successful result will be obtained within six to nine months. If there is no improvement within six months an anatomic abnormality is probably present and the patient should be subjected to operation. An anatomic abnormality is more likely to be present in a unilateral than in a bilateral case. In patients in whom there is no doubt that an anatomic abnormality exists it is unwise to wait for spontaneous descent, as degenerative changes begin in a retained testis at puberty.

**Chemotherapy in Measles and Whooping Cough.**—In an attempt to assess the value of chemotherapy in the prophylaxis and treatment of complications, Thompson and Greenfield divided 1,219 cases of measles and 244 of whooping cough into a treated and a control group. The treated group of patients included a high proportion of more severe involvement who received sulfanilamide or benzylsulfonamide regularly from admission, the dosage being graded according to age and increased if any complications developed. In this group fewer complications developed than in the control group, the difference being greatest in the aural complications of measles and in the pulmonary complications of both diseases, tending toward a reduced stay in the hospital. Toxic effects were mild and the drugs were well tolerated by children over prolonged usage. The drugs gave encouraging results in young children, especially in bronchopneumonia, otitis media and catarrhs of the upper part of the respiratory tract. Sulfanilamide appeared to be more effective than benzylsulfonamide. Although the results have been encouraging, due allowance must be made for the mildness of the recent measles epidemic and the authors suggest that this form of therapy might be given a wider trial in future epidemics of a more virulent character.

### Medical Journal of Australia, Sydney

2: 627-670 (Oct. 15) 1938

Oxygen Lack: Its Causes, Effects and Relief. H. W. Davies.—p. 627.

The Present Position of Surgery of Thyroid. H. R. G. Poate.—p. 635.

Review of the Problems of Suppurative Pteritis and of Its Surgical Treatment, Together with an Outline of the Prophylaxis and Treatment of Otitic Meningitis. D. G. Carruthers.—p. 644.

Cataract Dermatogenes, or Cataract with Neurodermatitis Chronica. A. L. Tostevin.—p. 647.

## Quarterly Journal of Medicine, Oxford

7: 495-592 (Oct.) 1938

- \*Anemia in Myxedema and Role of Thyroid Gland in Erythropoiesis. R. Bomford.—p. 495.  
 Staphylococcal Infections at Singapore. W. Hughes.—p. 537.  
 Hematopoietic Activity of Human Stomach in Pernicious Anemia. J. F. Wilkinson, L. Klein and C. A. Ashford.—p. 555.  
 Investigation into Treatment of Parkinsonism with Bulgarian Belladonna. N. S. Alcock and E. A. Carmichael.—p. 565.  
 \*Observations on Relation of Leukocytosis to Ascorbic Acid Requirements. T. D. Cuttle.—p. 575.

**Anemia in Myxedema and Erythropoiesis.**—Bomford presents the results of observations made on ten patients with myxedema and anemia and shows that the thyroid plays no direct part in erythropoiesis, that anemia in myxedema, unless complicated by a deficiency of iron or liver, is a physiologic adaptation on the part of the erythron to a diminished need of the tissues for oxygen, and that such effects of the thyroid on erythropoiesis as have been observed are indirect results of changes in the rate of metabolism. He observed that three types of anemia are found in association with myxedema. The simple hyperchromic type is the uncomplicated anemia of myxedema. It is considered to be part of a decrease in the size of the erythron, which takes place in hypothyroidism as a physiologic compensation for diminished need of the tissues for oxygen, and to be akin to the anemia which appears in animals exposed to atmospheres with a tension of oxygen greater than the normal. The other two types of anemia are the hypochromic and the addisonian hyperchromic anemias. These types are considered to be due to alimentary deficiencies of iron and liver, respectively. They differ from the simple deficiency anemias only in being modified in certain respects by the coexistence of myxedema. The simple hyperchromic type of anemia responds slowly to treatment with thyroid alone, in such doses as are found to keep the patient free from symptoms of myxedema or hyperthyroidism. The hyperchromic and addisonian hyperchromic types should be treated with thyroid and with adequate doses, respectively, of a preparation of iron or potent liver. The normal size of the erythron depends on the rate of consumption of oxygen by the tissues, as well as on the tension of oxygen in the atmosphere. This explains the recession of the red marrow up the cavities of the long bones as the animal grows and the rate of metabolism decreases. There is no evidence that thyroxine is one of the factors the presence of which in the bone marrow is necessary for the normal maturation of red cells. It is suggested that the thyroid affects erythropoiesis only indirectly, through its effects on the consumption of oxygen by the tissues and on gastric secretion.

**Leukocytosis and Ascorbic Acid.**—Cuttle investigated the relation between the leukocyte count in leukemia and the utilization of ascorbic acid and records the effect on ten patients of large doses of ascorbic acid as a therapeutic measure. All patients under investigation were given a carefully prepared diet containing approximately 30 mg. of ascorbic acid daily. In order to establish a base line an additional 25 mg. of ascorbic acid was given daily by mouth for nine days. For the remainder of the period of observation the patients received 1,000 mg. of ascorbic acid a day in divided oral doses of 500 mg. morning and evening. The excretion of ascorbic acid in the urine was estimated by the method of Harris and Ray. Ascorbic acid values for whole blood and plasma were estimated by the method of Farmer and Abt, as modified by Pijoan and Klemperer. The intradermal test for vitamin C deficiency, as reported by Rotter, modified for use in human subjects by Portnoy and Wilkinson, was tried during the course of this investigation. The test was fairly satisfactory in showing the trend of saturation but did not prove sufficiently accurate for the purposes of the study. During the period provided for a base line, three patients suffering from leukosis and three of the six of the control group had a daily urinary excretion of less than 13 mg. of ascorbic acid. It may well be that the other control cases would have reached the minimal standard excretion if the control period had been longer. The daily oral administration of 1,000 mg. in three cases of leukosis did not significantly increase the urinary

excretion of ascorbic acid during the first three days. In the control series the urinary excretion varied from 5 to 50 per cent on the first day and had risen to 50 per cent or more on the fourth day. In another patient with leukosis, 5,000 mg. of ascorbic acid was given intravenously and this led to the excretion of only 418 mg. in the urine. A normal person would be expected to excrete at least 2,500 mg. (Wright, Lilienfeld and MacLenathen, 1937). From 500 to 4,000 mg. of ascorbic acid was required to saturate the control patients. In the patients with leukosis the amount required was obviously much greater, and in fact saturation was never achieved during the period of leukocytosis. All patients, including the control series, showed low initial plasma and whole blood ascorbic acid levels (from 0.15 to 0.7 mg. per hundred cubic centimeters). The patients with acute and chronic leukosis and the six controls showed an abnormally low level of vitamin C nutrition. This shows that the maintenance of a minimal standard excretion and the response to a test dose of ascorbic acid alone are of little or no value in detecting the more marked degrees of vitamin C deficiency. Judged by the ascorbic acid requirements to produce saturation and the blood and serum levels of ascorbic acid, the controls behaved in a normal manner, for when given large doses of ascorbic acid (1,000 mg. daily) they became saturated within four days, with a urinary excretion of from 50 to 72 per cent of the daily intake. The response of patients with leukosis was abnormal, for the saturation point was never reached and the amount excreted in the urine was from 8 to 40 per cent. The accompanying leukocytosis affords only a partial explanation of the increased usage of vitamin C in infection, which is seen also in infections not associated with a leukocytosis; increased metabolism is probably an additional factor. There was no significant fall in the leukocyte count when the patients were receiving large doses of ascorbic acid alone. These observations agree with those of Gingold (1937) and Thiel (1938) but do not confirm the therapeutic results claimed by Eufinger and Gachtgens (1936). An increase in the number of platelets noted in one patient might be credited to ascorbic acid therapy if spontaneous remissions in thrombocytopenic purpura were not so common; however, Thiel (1938) has claimed that ascorbic acid raises the platelet count. The hemorrhagic state associated with acute myeloblastic leukosis was not affected by large doses of ascorbic acid.

## South African Medical Journal, Cape Town

12: 743-780 (Oct. 22) 1938

- Sulfanilamide in Treatment of Meningococcal Meningitis. J. A. Bell and W. H. Palmer.—p. 745.  
 Modern Therapeutics: The Wheat and the Chaff. C. H. Coetzee.—p. 748.  
 National Health Insurance: Some Comments on the Commission's Report. J. C. Gie.—p. 753.  
 The Separation of the Sphere of Action of Gynecologic and Obstetric Clinics from Other Clinics in the Hospital. F. Daels.—p. 755.  
 \*Influenza as a Factor in Heart Disease. E. E. Wood.—p. 759.

**Influenza and Heart Disease.**—During the last few years Wood has seen several cases of cardiac trouble which have been obviously caused by influenza. Four cases are recorded in which partial heart block was caused directly by influenza. In three further cases the heart was previously in an unsound condition but an attack of influenza caused partial heart block to be superimposed on the already existing condition. One case is included of regular nodal rhythm, as a direct result of influenza, in which the bundle of His appears to have escaped injury entirely. Attacks of influenza are so numerous and widespread that the majority of attacks can have little or no effect on the heart, but it is quite possible that those frequent cases of postinfluenza debility that are encountered are due to a mild and passing effect on the heart. The action of influenza on the healthy myocardium is mild, but it may produce a serious increase in a preexisting myocarditis and in some cases influenza may be the means of bringing to light a condition which had previously not been thought of or diagnosed. When symptoms point to an influenzal heart an electrocardiographic record is necessary as partial heart block, a frequent finding, cannot be diagnosed, although it may be suspected, without such a record. Treatment should be begun at once.

**Archives des Maladies du Cœur, Paris**

31: 885-984 (Sept.) 1938

- Consumption of Oxygen in Patients with Heart Disease, Particularly in Those with Mitral Defects. C. Laubry, D. Routier and Y. Bouvrain.—p. 885.
- Study of Symptomatology of Q Wave in Disorders of Coronary System. I. Chavez and L. Mendez.—p. 897.
- Phonocardiographic Studies on Patients with Aortic Arteriosclerosis. F. Tvaroh.—p. 910.
- \*Sedimentation of Erythrocytes in Course of Acute Articular Rheumatism (Bouillaud's Disease): Practical Value of Sedimentation Curve. L. Béthoux and R. Genin.—p. 946.
- Disturbances of Sinus Rhythm in Patient with Congenital Cardiopathy and Situs Inversus Totalis. J. Porto.—p. 960.
- New Formula to Foresee Normal Duration of Ventricular Systole. A. Sebastiani.—p. 973.

**Erythrocyte Sedimentation in Acute Rheumatism.**—Béthoux and Genin studied the curve of the sedimentation speed of the erythrocytes in all patients with acute articular rheumatism (Bouillaud's disease) who came under their observation in the course of the last four years. They found that the sedimentation speed is increased in the course of acute articular rheumatism. It is observed also in the course of various other acute febrile arthropathies and therefore cannot be utilized for the differential diagnosis of the diverse forms of acute polyarthritis. It does not constitute a diagnostic criterion of acute articular rheumatism except when this disorder, localized only in the heart, provokes evolutive attacks of "cardiac rheumatism"; in such cases the increase of the sedimentation speed of the erythrocytes allows one to suspect the rheumatic nature of the heart disease. The sedimentation curve is much more sensitive than the temperature curve and informs the clinician continually about the evolution of the infectious process which characterizes acute articular rheumatism. The prognostic significance of the sedimentation curve is not limited to the period of the active disease; it extends also to the convalescence, particularly as concerns the possibility of relapse. Frequently apyretic patients without visceral complications, who have no more articular pains and are considered cured, present nevertheless a slightly increased sedimentation index. The question arises whether it is necessary to await the return to normal before the patient is permitted to get up. Brahme, considering that the return to normal is often slow and that the absolute figure of sedimentation at the end of an hour is not an adequate criterion, proposes to take into account the hourly sedimentations determined after an interval of several days. This author suggested the formula  $R = \frac{S_2}{S_1 - S_2}$ ;  $S_1$  representing the figure of the first sedimentation and  $S_2$  that of the second sedimentation (taken after a week). If  $R$  is below 2 there will be no relapses; above 2 they are possible. Of thirty patients who were considered, seven in whom  $R$  was above 2.3 had relapses. While recognizing the interest of these researches and the simplicity of this formula, the authors think that the variations in the sedimentation speed during acute articular rheumatism present still too many unknown factors to place absolute confidence in it.

**Bruxelles-Médical, Brussels**

18: 1613-1642 (Oct. 23) 1938

- Recent Therapeutic Application of General Hyperthermia Produced by Physical Means. A. Bessemans.—p. 1613.
- \*Investigation of Blood Groups in Diagnosis of False Melena of the Newborn. M. Brouha and P. Moureau.—p. 1619.

**Blood Group in False Melena of Newborn.**—Brouha and Moureau report the clinical history of a mother and her newborn infant. Shortly after birth the child expelled meconium which was black with altered blood. These evacuations continued for four days and after that the stools were normal. At no time did the infant present signs of acute anemia. False melena was assumed. In trying to explain the pathogenesis of the false melena, the authors point out that in this case the delivery began with rupture of the amnion. They assume that at this time a quantity of blood entered the amniotic fluid and that during the twenty hours of labor the fetus swallowed amniotic fluid mixed with maternal blood. It is believed that this blood caused the melena in the nursing. In order to exclude definitely the fetal origin of the blood, tests were made

on the blood groups of mother and child. These tests revealed that the erythrocytes which were found in the bag of waters of this fetus were of maternal origin. Thus the diagnosis of false melena was corroborated.

**Journal d'Urologie Médicale et Chirurgicale, Paris**

46: 201-304 (Sept.) 1938

- Value of Chromocystoscopy in Diagnosis of Localization of Renal Tuberculosis. M. Secrétan.—p. 201.
- \*Some Considerations on Pathogenesis of Priapism. E. Chauvin.—p. 224.

**Pathogenesis of Priapism.**—Chauvin reports the clinical histories of two young men who consulted him on account of priapism. In the first patient, who had been married only nine days previously, there were no factors that would explain the disorder. The examination revealed that the priapism was not due to leukemia, to nervous factors or to neoplasia. After the erection had persisted for several days, an incision of the penis was decided on. When this was done the albuginea penis proved hard and of woody consistency. Its incision was followed by the discharge of black, sticky and thick but homogeneous and fluid blood. Careful inspection revealed nothing solid and no appreciable clot. A large quantity of blood was discharged and it seemed that the two cavernous bodies were emptied simultaneously through the incision on the left side. However, an incision was made also on the right side and care was taken that the evacuation was as complete as possible. As the blood was discharged the penis became soft again. The postoperative course was uneventful. An examination six weeks after the intervention revealed an entirely normal penis, but erection had so far remained impossible. The second patient had sustained a slight perineal trauma in the course of bicycling and, in the absence of other causes that might explain the continuous erection, it appears that this trauma might have had an etiologic role. In this case the author again resorted to the incision of the penis, but this time the blood that was discharged from the cavernous bodies was normal in color and in fluidity; there were no traces of clots and no signs of pitchy thickening. The discharge of the blood did not result in the cessation of the erection; in fact, the erection persisted for a considerable time after the intervention. Inspection two months after the operation revealed that the penis was normal in volume and consistency. In his extended discussion of the pathogenesis of priapism, the author takes up four points: (1) nervous factors, (2) disturbance in the venous backflow, (3) hematoma of the penis and (4) thrombosis of the corpora cavernosa. He reaches the conclusion that priapism is due neither to a hematoma of the corpus cavernosum or to an obliteration of the veins of the penis but rather to an obstruction of the venous capillaries by thickened and viscous blood. Abnormally prolonged erections, either pathologic (myelopathy) or physiologic (genital excesses) are the cause of this condensation of the blood, which is probably favored by certain prior conditions such as leukemia or hyperviscosity of the blood. This manner of regarding the condition has the great advantage of bringing all types of priapism within the same framework and of suppressing the purely etiologic distinction which the symptoms and especially the evolution, identical in all cases, do not justify.

**Presse Médicale, Paris**

46: 1593-1608 (Oct. 29) 1938

- Fundamental Lesions of Experimental and Human Mineral Pneumoconiosis. A. Policard.—p. 1593.
- \*Combined Galactose and Water Test as New Functional Test of Hepatic Insufficiency. F. Pollak.—p. 1596.

**Galactose and Water Test of Hepatic Insufficiency.**—Pollak cites his experiences with a combined galactose and water tolerance test. The procedure of the combined water and galactose test permits one to determine simultaneously the elimination of the liquid and the absolute and proportional elimination of galactose as well as the length of time necessary for each of these phenomena. Numerous investigations of this type have indicated that the duration of the elimination is of essential importance for the interpretation of the galactose test. The author describes and evaluates experiences with the combination galactose and water test in eight cases. Sum-



marizing his observations, he says that in the combined galactose-water test the elimination of galactose by the urine requires in healthy subjects, at the most, ninety minutes. If the elimination exceeds this time limit, this is an indication of a lesion of the hepatic parenchyma. The duration of the elimination represents a reliable criterion, independent of extra-hepatic factors. The reliability of the criterion can be proved by repeated control tests on the same person; it can be observed that there are considerable oscillations of the percentage and especially of the absolute elimination of galactose, close to the constancy of the duration of the elimination. The author concludes that it is possible to admit a simplification of the galactose test, in which the presence of sugar in a series of specimens of urine suffices to reveal a hepatic lesion, without a diminution in the reliability and sensitivity of the functional test.

### Archiv für Verdauungs-Krankheiten, Basel

63: 177-248 (Sept.) 1938

- \*Action of Vitamin A in Gastric Disorders. H. J. Kluth.—p. 177.  
Comparative Examination of Hydrogen Ion Concentration (pH Value) of Saliva and of Gastric Juice in Patients with Gastric Disorders. F. Stengel.—p. 191.  
Catamnestic Survey of Causes of Gastritis. K. Ilg.—p. 196.  
Visualization of Gastric Mucosa with Especial Consideration of Roentgenstereogram. Gertrud Schulze.—p. 220.

**Vitamin A in Gastric Disorders.**—Kluth says that he studied the action of vitamin A on ninety-six patients with gastric disorders such as various types of gastritis and ventricular and duodenal ulcers. At first the vitamin A was given three times daily by mouth in the form of dragées. Later the oral medication was combined with intramuscular injections (three times each week). However, the injection treatments were later discontinued because infiltrations were repeatedly observed at the site of injection. In reviewing the results that were obtained with the vitamin A therapy, the author says that favorable results could be obtained only in anacid and subacid gastritis. Cases of hyperacid gastritis and of duodenal and ventricular ulcer remained uninfluenced by vitamin A. The author shows that in this respect his observations differ from other reports in the literature. In cases of achylia, free acid appeared only following the injection of vitamin A. In some of the patients increases in weight were observed. Especially noteworthy was the favorable effect on the intestinal activity in constipation as well as in diarrhea. Discussing the mode of action of vitamin A, the author says that it is most probable that in patients with gastric disorders a vitamin A deficiency exists because of deficient resorption in the intestinal tract. This assumption is supported by investigations on the occurrence of night blindness in anacid gastritis and by the fact that these cases of night blindness can be influenced by the injection of vitamin A.

### Archivio Italiano di Chirurgia, Bologna

49: 117-200 (July) 1938. Partial Index

- External Functions of Pancreas in Relation to Unilateral and Bilateral Adrenalectomy. G. Cosentino.—p. 117.  
\*Metabolism of Hemoglobin After Surgical Interventions, Especially Gastric Resection. C. Scartozzi and M. Ferrando.—p. 133.

**Metabolism of Hemoglobin After Gastric Resection.**—Scartozzi and Ferrando observed the metabolism of hemoglobin after surgical operations, especially gastric resection. The latter operation was performed on fourteen of fifteen patients suffering from gastroduodenal or duodenal ulcers. The observations were made before the operation, fifteen days later and again at a given date which varied from four to six months after the operation. Six normal persons who had been operated on for appendicitis or hernia served as controls. The authors found that patients suffering from gastroduodenal or duodenal ulcers have diminished metabolism of hemoglobin and diminished formation of bile salts. The metabolism of hemoglobin increases immediately after a surgical operation. The increase, however, is transient. The values of hemoglobin and bile salts formation gradually decrease during the first four or six months after the operation. By this time the substances become almost normal and stop decreasing without returning to the low values which existed before the operation. The authors conclude that

the fear for the development of hemolysis and grave forms of anemia after ample gastric resection is both unjustified and exaggerated. The operation is frequently followed by transient hemolysis and by benign, curable and uncomplicated forms of anemia.

### Clinica Medica Italiana, Milan

69: 575-646 (Sept.) 1938

- \*Nitrogen Metabolism in Primary Progressive Muscular Dystrophy. A. Guarnaschelli-Raggio.—p. 577.  
Considerations on Syndromes of Thrombopenic Hemorrhages. B. Nelli.—p. 603.  
Tumors of Reticulo-Endothelial System: Cases. G. Rocchini.—p. 625.

**Nitrogen Metabolism in Muscular Dystrophy.**—Guarnaschelli-Raggio observed the curve of elimination of nitrogen in the urine of eleven patients, children and adults, who had primary progressive muscular dystrophy. The determinations were made before and after administration of a pancreatic extract. The patients were fed a diet rich in proteins from one week before the first determination up to the end of the observations. The author found that the daily elimination of nitrogen through the urine is diminished in all cases (an average of 0.04 or 0.05 Gm. of nitrogen in the total amount of urine eliminated in twenty-four hours). The amount of eliminated nitrogen frequently changes, regardless of the fact that the daily intake of proteins in the diet of the patients is constant. The patients suffer from disturbances of the pancreatic digestion and the intestinal absorption of proteins. The metabolic disorders are the same in the various clinical forms of the disease (atrophic, pseudohypertrophic, juvenile, facial, scapular and humeral and mixed forms). The diminished elimination of nitrogen is more intense in grave forms (those of an early rapid evolution) than in benign forms of the disease. Administration of a daily dose of pancreatic extracts for one or two consecutive months, in association with a diet rich in proteins, increases the amount of nitrogen eliminated in the urine. Coincidentally the general condition of the patients improves and the pancreatic and intestinal disturbances subside (as shown by the basal metabolism, which becomes normal). The author concludes that the disease is caused by a deficient supply of nitrogen in the body which originates in alterations of the intestinal absorption of proteins from functional disorders of the pancreas. Continuous administration of a treatment with pancreatic extracts up to normalization of the elimination of nitrogen in the urine induces permanent satisfactory results except when irreparable damage has taken place. The best results are obtained from early treatment. The author used a preparation of pancreatic extract (Richter) in daily doses of 60 or 100 drops for one or two consecutive months. Discontinuation of the treatment was decided by normalization of the nitrogen elimination, which took place in one or two months except in one case in which treatment failed.

### Brasil-Medico, Rio de Janeiro

52: 961-982 (Oct. 22) 1938. Partial Index

- \*Use of Standard Blood Plasma in Classifying Blood Groups. H. Maciel.—p. 961.  
Proteins. M. E. de Souza Aranha.—p. 971.

**Standard Blood Plasma in Classifying Blood Groups.**—Maciel states that standard blood serums which are prepared for use in classifying donors for blood transfusion deteriorate in about one month when they are at room temperature and in about three months when they are kept in the icebox. Deterioration is the cause of shock from transfusion and of false results in relation to mutability of blood groups. The latter never change. At first the author used freshly prepared blood serums which were taken from the icebox only for immediate use. No case of shock from transfusion was observed. Later on he found that the agglutinating power of the blood plasma is more intense and lasting than that of the blood serum. Since then he has used freshly prepared blood plasma in the conditions mentioned. The stock is renewed every three months, the old stock being disposed of. The author points out the advisability of making determinations of the agglutinating power of the blood plasma (or blood serum) which

is going to be used as a standard in classifying donors, separately from those which are done in the blood, because of the fact that frequently in the blood of persons of the B group the globules but not the plasma and the serum are rich in agglutinins. If good standard blood plasma (or blood serum) of the A and B groups is available, verification in blood plasma (or blood serum) of the O group is unnecessary.

### Revista de la Asoc. Med. Argentina, Buenos Aires

52: 951-1014 (Sept. 30) 1938. Partial Index

Hemorrhagic Ulcerated Syphiloma of Stomach. J. A. Caeiro and A. E. Bianchi.—p. 951.

Pyelitis of Pregnant Toxicosis Form. E. Thwaites Lastra, A. M. Brea and R. Bizzozero.—p. 955.

\*Treatment of Acute Nephritis in Children. F. de Filippi.—p. 957.

Action of Calcium Chloride on Poisoning by Cocaine and Succedaneous Preparations. R. E. Carratalá and A. Buzzo.—p. 966.

Suggestions for Treatment of Malignant Granuloma. F. R. D'Ovidio.—p. 974.

**Acute Nephritis in Children.**—Vollhard's treatment consists in suppression of food and of the water intake and administration of small quantities of orange juice for from five to six days. De Filippi reports satisfactory results from the treatment in a large number of children who were suffering from acute diffuse glomerulitis. Seven cases are reported. A cathartic of castor oil or magnesium sulfate is given to the patients immediately before starting the treatment. Orange juice is administered alone for the first five or six days and then in association with food and water for one or two more weeks. The daily allowance increases from 75 or 100 cc. of orange juice during the first two days to 600 cc. during the last three days and also during the following two weeks in which the diet is reestablished. The arterial pressure, weight and diuresis are determined before and in the course of the treatment. As a rule the arterial pressure and diuresis become normal and edema diminishes within two or three days. The loss of weight depends on the lowering of edema. Hematuria diminishes early in the course of the treatment, except when due to focal infection, which must have the proper attention. The diet is slight during the first week in which it is reestablished and slowly increases so as to be normal by the end of the second week. The treatment is well tolerated. Acute cardiac and renal complications or the development of chronic renal disease do not follow. Permanent recovery takes place within three weeks or a month in all cases of acute and sub-acute forms in which there are no complications.

### Deutsches Archiv für Klinische Medizin, Berlin

182: 477-636 (Oct. 6) 1938. Partial Index

Kymographic and Electrocardiographic Aspects of Sport Heart. H. Reindell.—p. 506.

Vitamin C and Diabetes. H. Bartelheimer.—p. 546.

Action of Baths and Febrile Conditions on Elimination of Porphyrin. U. Graff.—p. 556.

\*Duodenitis. H. Schnetz.—p. 570.

Are There Transitions Between Recklinghausen's and Paget's Disease? A. von Domarus.—p. 611.

Formation of Fat from Carbohydrates in Fat Organs. K. Felix and W. Eger.—p. 623.

**Duodenitis.**—Schnetz thinks that duodenitis should be recognized as an independent disease entity. To be sure; its isolated occurrence is rare; it concurs with secondary functional pancreatic disorders, with functional disturbances of the stomach and most frequently combined with other organic diseases of the epigastric region. The author shows further that in cases of gastric ulcer, in disorders of the biliary passages and in pancreatopathies the syndrome of duodenitis should receive diagnostic and therapeutic attention. On the basis of reports in the literature and of his own observations, he shows that the diagnosis of the syndrome of duodenitis can be based on the demonstration of products of inflammation in the duodenal contents, on the relief visualization of the duodenal mucosa and on the detection of pancreatic symptoms with clinically demonstrable disturbances of the digestion and of the internal secretion. Pancreatic symptoms are detected so frequently in the course of duodenitis that they have an important part in the diagnosis. The existence of a disturbance in the external secretion of the pancreas in duodenitis is proved not only by the complex of pancreatic symptoms but by the

demonstration of an increase in the duodenal juice, of an inhibition in the amylase and of a disordered secretion of trypsin in the functional test of the pancreas according to Berger and Hartmann and by the examination of the sugar metabolism according to Schnetz. In the clinical aspects of duodenitis the pancreatic disturbances have the main part; they are regarded chiefly as functional. An attempt was made to determine the correlations between duodenum and pancreas and to differentiate between duodenitis as the cause of functional disturbances of the pancreas and of duodenitis as the cause or result of organic diseases of the pancreas. Discussing the treatment of duodenitis, the author says that aside from the treatment of possible causes (sympathetic dystonia, thyrotoxicosis, intestinal infections, disorders of the biliary tract and gastrointestinal ulcers) the therapy should aim at reducing the load on the digestive system by means of dietetic treatment. Moreover, he obtained favorable results by a combination therapy with pancreatic ferments and vitamins C and B<sub>1</sub>.

### Deutsche Zeitschrift für Nervenheilkunde, Berlin

147: 217-292 (Oct. 11) 1938

Histopathology and Pathogenesis of Fatal Insulin Shock. G. Döring.—p. 217.

Heredodegeneration Difficult to Classify. J. Dreter.—p. 228.

\*Myeloma and Nervous System. I. Scheinker.—p. 247.

Classification of Polyradiculitides. A. Juba and F. Kovács.—p. 274.

**Myeloma and Nervous System.**—Following a general discussion of various types of myeloma, Scheinker reports the clinical history of a man aged 38 with a disorder involving the skin and the nervous system. The author thinks that the disease process in the peripheral nerves represents a new form of interstitial polyneuritis. Summarizing the observations described in this paper, he says that the patient had a "solitary" plasmacellular myeloma that was localized in the sternum. The case disclosed a connection between a disease of the bone marrow that was accompanied by metabolic disturbances and a peculiar cutaneous and nervous disorder. The cutaneous disorder became manifest in a coarse-fibered transformation or an increase in the connective tissue in the region of the cutis and the subcutis. The disease of the nervous system presented the clinical aspects of an ascending polyneuritis of the type of Landry's paralysis. The anatomic basis of this polyneuritis was found to be a hitherto unknown disease of the peripheral nervous system. It was characterized by a severe proliferation of the perineural or epineural connective tissue and by a consecutive parenchymal disease of the nerve fiber. On the basis of the histologic characteristics the author suggests that the term "perineuritis interstitialis scleroticans" be applied to this form of polyneuritis. He assumes a causal connection between the disease of the bone marrow and the peculiar cutaneous and nervous disorder and suggests that toxic metabolic waste products which are characteristic for myeloma may cause such cutaneous and nervous changes. He believes that the pains which dominate the clinical picture of myeloma are caused in the majority of cases by toxic impairment of the peripheral nerves.

### Klinische Wochenschrift, Berlin

17: 1497-1528 (Oct. 22) 1938. Partial Index

Arteriovenous Anastomoses in Animals and Man. L. Aschoff.—p. 1497.

Vitamin A Deficiency and Thrombocytic Reaction. E. Lorenz.—p. 1498.

Leukopenia Following Intravenous Administration of Colloidal Carbohydrates. H. Staub, K. Mezey and G. Golasz.—p. 1501.

Depot Insulin in Treatment of Diabetes in Children. F. Linneweh and Marga Eitel.—p. 1507.

Significance of Skin in Defense Against Infectious Diseases. H. Knauer.—p. 1510.

\*Significance of Allergy for Endocrine Arthritis. A. Sylla.—p. 1511.

**Allergy in Endocrine Arthritis.**—Sylla says that in the majority of cases of so-called endocrine arthritis neither the pathomorphologic changes nor the localization of the process is of decisive importance. The localization seems to depend on a hereditary or acquired predisposition. In the majority of cases the disease is an inflammatory process that originates in local foci. The endocrine factor involves a reduction in the reaction capacity of the diseased tissues as well as of the entire organism. Insufficient production and secretion of hormones reduces the reaction capacity. This implies that in case of insufficient production of certain incretions the allergy is

influenced in the negative direction, so that now, in case of inadequate reaction, the inflammation takes a chronic course, below the threshold. Administration of the lacking glandular principles influences the metabolic and allergic reactivities in the direction of a greater sensitivity and a more lively response to stimulation. Consequently the treatment must aim to effect sensitization by the administration of the lacking substances and then, in combination with the usual physical and hydrotherapeutic methods, to effect improvement or even cure of the articular disorder. To what extent glandular hyperfunctions influence articular processes has not been clarified as yet. It is possible however that, for instance in severe hyperthyroidism, hyperergic reactions might play a part. Nevertheless the articular disturbances in which hyperfunctioning of the endocrine glands plays a part are doubtless much less frequent than those endocrine arthritides which, although not caused, are greatly influenced by glandular hypofunction.

### Zeitschrift für Kinderheilkunde, Berlin

60: 181-284 (Oct. 15) 1938. Partial Index

- Agglutinin Formation in Whooping Cough and Immunobiologic Study on Rachitic and Nonrachitic Children. F. Hansen.—p. 181.  
\*Experiments with Wheat Germ Oil (Vitamin E) in Care of Premature Births. F. Widenbauer.—p. 216.  
Clinical Aspects of Congenital Stridor. E. Traub.—p. 222.  
Erroneous Diagnoses in Vesicular Emphysema in Lung of Child. W. Matheja.—p. 236.  
Pharyngitis of Scarlet Fever in Infants. W. Brenner.—p. 243.  
Problem of Still's Disease. M. Schwaiger.—p. 255.

**Vitamin E in Premature Infants.**—Widenbauer raised the question whether premature infants might perhaps suffer from a deficiency in vitamin E resulting from a vitamin E deficiency in the mother. This possibility seems justified in view of the reported success obtained with vitamin E in the prophylaxis and therapy of habitual abortion and of the tendency to premature births. If women who are subject to abortion and premature births have a deficiency of vitamin E, it may be reasoned that the infant too might have such a deficiency. It has been proved by Emerson and Evans that vitamin E influences growth and so Widenbauer decided to investigate the effects of small quantities of wheat germ oil (vitamin E) on the growth of premature infants. A rapid increase in weight induced by vitamin E after prolonged arrest of the growth was regarded as the criterion of the action of vitamin E. Since changes in feeding and care and the existence of infections would obscure the results, such cases were excluded in the estimation of the action of wheat germ oil. Consequently only a comparatively small number of cases could be selected in two years. Seventeen premature infants were treated with wheat germ oil and two premature infants served as controls and were given olive oil. In eleven of the seventeen premature infants the vitamin E produced a rapid increase in weight after a previous arrest in growth, and thus it seems possible that the wheat germ oil does promote the growth of premature infants. To be sure, the comparatively small material permits no definite conclusions, but the results obtained so far justify further investigations.

### Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

82: 4777-4952 (Oct. 1) 1938. Partial Index

- \*Value of Quinine as Prophylactic Against Influenza. N. H. Arkema.—p. 4789.  
Circular Strictures of Vagina. R. F. Schuurmans.—p. 4799.  
Metal Tourniquet. V. Winters.—p. 4802.  
In Memory of Boerhaave. D. Schoute.—p. 4807.  
Boerhaave's Influence on American Medicine. H. E. Sigerist.—p. 4822.  
Hermann Boerhaave as Clinician. I. Fischer.—p. 4835.

**Quinine as Prophylactic Against Influenza.**—Arkema studied the prophylactic value of quinine against influenza in four infantry regiments. Two of these regiments were subjected to prophylactic treatment with quinine and the two others were not. Summarizing his observations, he says that in comparing the two regiments (5 and 16) in which quinine prophylaxis was employed with those (18 and 21) in which this was not done, it can be seen that the first two regiments had a much smaller number of influenza patients and considerably fewer complications than the two others. However, this difference is due chiefly to the large number of influenza cases in regiment 21. Regiment 18, in which quinine prophylaxis was

likewise omitted, did not have a larger number of influenza cases than the two regiments (5 and 16) which had been subjected to quinine prophylaxis. Moreover, records revealed that regiment 21 had had a comparatively large number of influenza cases in three previous years. The author concludes from this that in the population from which the members of the twenty-first regiment are drawn there must be factors which are responsible for the high incidence of influenza. Thus the observations made so far by the author do not furnish a convincing proof for the value of quinine in the prophylaxis of influenza. In view of the peculiar role assumed by regiment 21 in these investigations, the author intends to use quinine prophylaxis next year in this regiment and thereby determine whether it will reduce the incidence of influenza and thus furnish a better insight into its prophylactic value.

### Hospitalstidende, Copenhagen

81: 1049-1080 (Nov. 1) 1938

- Investigations on Sulfate Clearance. T. Bjerling and E. Øilgaard.—p. 1049.  
\*Investigations on Action of Nicotinic Acid in Experimental Gastroprival Pellagra: Preliminary Report. S. Petri, F. Nørgaard and E. Bandier.—p. 1068.

**Nicotinic Acid in Experimental Pellagra.**—Petri and his associates found that in experimental gastroprival pellagra in swine, contrary to the result in pellagrous conditions produced in swine experimentally by feeding, nicotinic acid is without effect. In one case in which the pylorus was resected, the subpellagrous symptoms disappeared following the administration of nicotinic acid. The authors say that the effectivity of the agent seems to depend on the presence of a gastric function (an "antipellagra factor").

### Nordisk Medicinsk Tidskrift, Stockholm

16: 1647-1686 (Oct. 22) 1938

- Tuberculosis in Eskimos in Angmagssalik, East Greenland. A. Høygård.—p. 1647.  
\*Mercuric Oxycyanide Intoxication. O. Berner and E. Jensen.—p. 1656.  
Points of View Regarding Modern Hospital Ventilation and Heating. C. Naeslund.—p. 1660.

**Mercuric Oxycyanide Intoxication.**—Berner and Jensen report the case of a woman who drank a 3 per cent solution of mercuric oxycyanide and died three hours later. Necropsy and chemical analysis of the intestinal contents disclosed death from prussic acid poisoning. Most cases of mercuric oxycyanide intoxication, they say, behave like ordinary mercury poisoning; only in exceptional cases is this type of intoxication confused with prussic acid poisoning. Story and Lorenz have recently called attention to the part played by the hydrochloric acid in the gastric juice in the development of prussic acid poisoning. Twenty cc. of a 3 per cent solution of mercuric oxycyanide will set free 106 mg. of prussic acid. The result of the poisoning depends on the amount of the mercuric oxycyanide solution taken and the degree of gastric acidity, together with the rapidity with which the resorbed prussic acid is rendered harmless. Even a two hundredth normal solution of hydrochloric acid will instantly set free prussic acid, and the presence of relatively abundant gastric juice and a suitable amount of mercuric oxycyanide in proportion to the amount of gastric juice affords the best condition for the occurrence of prussic acid poisoning.

### Ugeskrift for Læger, Copenhagen

100: 1127-1146 (Oct. 6) 1938

- Tetany and Parathyroid Insufficiency. H. Nielsen.—p. 1127.  
\*Investigations on Effect of Administration of Nicotinic Acid in Two Patients with Idiopathic Steatorrhea (Sprue). J. Bing and B. Broager.—p. 1131.  
Treatment of Pellagra with Nicotinic Acid: Review and Report of Case. O. Bernth and G. K. Stürup.—p. 1137.  
Pellagra Treated with Nicotinic Acid: Case. J. Ravn.—p. 1140.

**Nicotinic Acid in Idiopathic Steatorrhea (Sprue).**—Bing and Broager found that nicotinic acid had a marked effect on the water content quantity and the consistency of the feces in two cases. There was no increase in the resorption of dry substance, lipid, nitrogen, calcium or ascorbic acid, and none of the other symptoms of sprue were affected in the same distinct manner as the diarrhea. On discontinuing the medicament diarrhea again set in.

# THE STUDENT SECTION

of the

## Journal of the American Medical Association

*Devoted to the Educational Interests and Welfare of Medical Students, Interns and Residents in Hospitals*

SATURDAY, DECEMBER 24, 1938

### Practical Pointers and Pitfalls in Medical Practice

J. M. ROBB, M.D.

DETROIT

The pitfalls in the practice of medicine depend to a large extent on what the future holds in the method and the manner of this practice. If state medicine is to be the future, I should discuss with you (1) how to make blanks in triplicate or quadruplicate, (2) how to build political fences, (3) how to kotow to political bureaucracies, (4) how to appease the sadistic boss who likes to see the fellow beneath him wriggle, (5) how one doctor may treat 100 patients a day, (6) how a look and a bottle constitute a consultation and how to steel one's conscience to this, (7) how to ignore the malingerer in order to have some time to comfort the really sick, (8) how to build a nonprofit insurance company and (9) how to become a physician to end physicians.

Some alleged weaknesses of our present system may be overcome. But will not many serious evils arise to confound further and deter us in our efforts to help the sick and suffering? There is no group of people in the world that appreciates more than we do the following statement: "There is but one permanent thing in the world, and that is change." On the other hand, there is no group who understands more clearly than we do that this change must be by slow evolution and that this slow evolution must be directed by the pilot who flies the plane of medicine in actual combat with disease.

I believe that the pioneer spirit of America survives in the practicing physician of today more nearly than in any other profession or calling. The pioneer was accustomed to hardships and so must be the physician. "He calls no hour of day or night his own, through heat and cold he goes his rounds alone." And although as individualistic as he needs be, I believe that as a group he will fight to the last ditch those vicious radicals who are trying to stop him. I said "practicing" physicians advisedly. Men in institutional work are contributing their share to the research field of medicine. Most of them, by lack of experience, are unfamiliar except through hearsay with the demands of actual practice. If you have chosen

the cloistered field of scientific research, what I have to say may bore you for the present, but even for you it will have a purpose; namely, to make you more cognizant and tolerant of your struggling professional brother—the doctor in the field. What has he given to America? What is our heritage? By what means may we emulate him? For we do want to follow in those hallowed footsteps of the practitioner of a free America, and therefore my emphasis will be placed on the exposition of those qualities that I feel make the American doctor without a peer.

This is a day of specialists—and we need them—but we also need the "family doctor" not only because of what he gives to the community but also because from him we may learn those human attributes which constitute the art and practice of medicine. May I name some of these factors which identify the good doctor in all fields and that go to make a good practitioner? Aphorisms, perhaps, but at least pegs on which to hang your thoughts for rather permanent mental reference. These may be mentioned as follows: availability, ability, personal appearance, punctuality, sportsmanship, postgraduate study and personality. From an inculcation of these attributes should develop a proper concept of where you should locate to practice, of how your prescriptions are written or how well your office looks, or perhaps the choice of your secretary or it may be your club memberships—in fact, many other problems of decided interest to the young man beginning in practice. Many of these I will not have time to discuss.

#### AVAILABILITY ESSENTIAL

One of the first and most essential demands of a good practitioner is availability. Of what use is outstanding ability if that person of ability cannot be found? It is therefore necessary that the office be the center of attraction, particularly for the first ten years in actual practice. We all appreciate the economic, social, educational, industrial and religious effects and demands on the lives of the doctors, and to these he must give some attention. Nevertheless he must concentrate on the subject for which he has spent so many years in training.

It requires much self sacrifice I confess, but if you are to build a niche for yourself you must deny yourself. One aphorism that may be used here is "Think only of yourself if you want others to forget you."

The second factor I wish to discuss is ability. It must be assumed that, with the educational standards as high as at the present, you must have had ability to have gotten this far along the road to success. You are now ready to put that training to the test, and although books are a necessity and a maximum of theory must be accumulated, Osler's warning may well be applied; that is, "To study the phenomenon of disease without books is to sail an uncharted sea; while to study books without patients is not to go to sea at all."

The third attribute in importance I wish to discuss is personal appearance, and of course in the practice of medicine this means a professional appearance not alone in apparel but in manner. It is necessary that you have the appearance of self control and self reliance, to inspire confidence. This does not, however, permit you to dress so that the man in the street might be inclined to step up and ask you "Where are the races?" This garb makes a distinctly bad impression. It is always well to keep in mind the old adage "Blacken a man's shoes if you want to keep him out of the mud. The man with dirty shoes doesn't care where he walks." It is necessary that you keep polish on your personal appearance—on your professional appearance—as well as on your mental and moral habits.

Punctuality is another attribute that is too often forgotten. The nature of your work is

inclined to give you a good excuse for being late. Don't abuse this privilege and make of it an alibi. If it is your job to be at a certain place at eleven in the morning, be there or telephone. Don't forget that every one is watching you, not just a few of your friends. And in this regard, in considering punctuality, "Throw away your wrist watch and buy an alarm clock."

Sportsmanship is something to be remembered. Medicine is a hard mistress, and there are many temptations which come to you through your practice. Always remember "If you throw mud, you lose ground." Therefore be slow to criticize, for much depends on a difference of opinion. Become connected with your medical societies, meet the men in your profession and realize that you owe some of your time to the upbuilding of the profession to which you belong. Let me repeat to you that we are individualists; nevertheless a proper contact with your medical organizations, with societies outside medical interest, will bring to you a greater concept of the needs and wishes of the community in which you live.

Next, aim at a professional perfection by writing papers, following postgraduate pursuits, realizing always that there is plenty of room in the world for successful men. "Ideals are like stars; you will not succeed in touching them with your hands, but like the sea-faring man on the desert of waters, you choose them as your guide and follow them, reaching your destiny."

And, last of all, don't forget personality. A cheerful face soothes many a fevered brow, and a merry heart doeth good like medicine.

## Comments and Reviews

### TRENDS IN MEDICAL INVESTIGATION

*Abridgment of a paper by Dr. Roger I. Lee of Boston, read before the American College of Physicians, New York, April 4, 1938, and published in the Annals of Internal Medicine, November 1938.*

Truly the advances in medicine have been prodigious in the last few generations. The changing situation has developed in internal medicine new attitudes and new standards. It is not too much to say that a new specialty has appeared, that of the medical investigator. In these bewildering changes there seems at times to be a restless activity of feverish intensity. Granted that the internist should be a medical investigator, should his work be evaluated on actual publications, on quantity of publications, and what are some of the necessary criteria for the scrutiny of the quality? Or has there not developed a technic in medical investigation

that is stereotyped, narrow and inadequate? It should be possible to pause in order to strengthen some of the points of weakness of the present system. Careful objective observation must be the foundation of any investigation. But unless the scope of these observations is carefully planned and the experiments carefully designed, the labor may be wasted. Indeed the critical observation or experiment is relatively rare. We have to admit that in the large majority of instances the design or plan or observation or experiment is so bad or inadequate that the entire procedure is valueless.

The myth of the athletic heart is an excellent example of a product of faulty observation, of the failure to understand and use ordinary statistical principles and of faulty reasoning, especially in the conclusions based on the physiologic principle that muscular exercise increases the size of the heart. Somehow erroneous obser-

variations appeared in print aiming to show the increase of the heart under athletic training, especially in colleges. A few cases of cardiac disease or death were cited to furnish the statistical evidence. Then extraordinary conclusions of all sorts were made. However, instruments of precision showed the original observations to be erroneous. But the myth was kept alive by a credence in the statistical evidence although this evidence satisfied no statistical requirement. It is difficult to secure adequate data to meet any reasonable statistical requirements for the proof that athletic training in youth predisposes to cardiac death from twenty to forty years later. A little thought indicates many other factors that might affect the heart in addition to college athletics. Of course, any conclusions based on such faulty observations and statistics are worthless. Unfortunately the myth still lives, though in a feeble state.

#### IMPORTANCE OF OBSERVATION

Much has always been made of the importance in medicine of observation. Every medical student is impressed by the paramount necessity of the trained use of touch, sight, hearing, smell and occasionally of taste. There are many mechanical devices to assist those senses. But in the rush of medical progress other faculties are needed to supplement these observational senses. Hippocrates and his group were masters in the art and science of observation. But the conclusions of Hippocrates, while based on accurate and repeated observations, were arrived at by deductions that were as carefully controlled as the observations themselves. Likewise, Jenner observed cowpox in milkmaids. By the simple statistical collection of these data, Jenner noted in a sort of statistical fashion that most milkmaids contracted cowpox. His statistical data showed that smallpox was rare among milkmaids; or, in other words, there was a high correlation between the incidence of cowpox and the absence of smallpox. Jenner next called on another trait and deduced that the cowpox protected against smallpox. If his observations were correct and if there were no unknown disturbing factors, this deduction was logical and it was so subsequently proved by the accumulation of abundant statistical data and the establishment of a high correlation of absence of smallpox and the presence of cowpox.

In some ways, medicine has not changed in the development of the use of statistics or the use of deduction since the days of Hippocrates or of Jenner. We have done decidedly better with regard to statistics than with regard to deductive reasoning. It took a long time to realize that mortality figures in pneumonia had to be broken up into age groups and also into types of the infecting pneumococcus; then

there may be a yearly or seasonal variation. Nevertheless many assert that, irrespective of statistics, certain procedures in pneumonia do good. At one time, based on electrocardiographic evidence, the use of digitalis was advocated in every case of pneumonia. Without statistical proof and without sound reasoning, the use of digitalis became practically routine in the treatment of pneumonia. Subsequently clinical studies under adequate statistical control indicated that the routine employment of digitalis was actually detrimental in the average case.

It is the fashion to deride statistics, but the observational data which go into the statistical treatment, like the beef that goes into the can, are not changed by the process. The method is less faulty than the data. It is a long road to prove statistically the benefit of a therapeutic procedure in pneumonia. Very likely there are other unrecognized variables besides age groups and types of pneumococci. Animal experiments and test tube research are illuminating, but the final answer to the query of the beneficial effect of a procedure in pneumonia in human beings must be statistical.

If data do not meet simple statistical requirements, it is futile to try to draw conclusions from them. While many of our medical errors are derived from failure to use statistics correctly, nevertheless the greater bulk of medical errors are derived from faulty reasoning. We make many unjustifiable assumptions. Improper conclusions or deductions may be readily made from data which are accurate enough. For example, it was argued for many years that, since malaria existed in marshy places, it was the dampness which caused the malaria.

#### FAULTY REASONING

There is one form of faulty reasoning or faulty logic which is common in medical literature. For example, it is known that all cases of pernicious anemia have an absence of free hydrochloric acid in a gastric analysis. It does not follow, however, that pernicious anemia exists in all cases in which hydrochloric acid is absent. Again, most of the cases of pernicious anemia respond to liver therapy. It may be argued that liver therapy is a therapeutic test for pernicious anemia, but one must not argue that no cases are to be diagnosed as pernicious anemia if they do not respond to liver therapy and that therefore liver therapy is always successful in pernicious anemia.

From the very nature of things, clinical observations are complicated. There are always unknown variables. Nevertheless, clinical material has always furnished excellent illustrations of the best and most scientific types of medical investigation. A great many medical beliefs, medical procedures and the like are based on



what we call the results of logical reasoning. As an example, is it logical to assume that a person infected by typhoid bacilli in the water will be less sick than a person infected with typhoid bacilli in milk? Presumably the milk will carry more bacilli than the water. Let us grant that the virulence of the micro-organisms is the same and that the series of cases is large enough to iron out the variability of possible special groups of immunes or partial immunes. The answer must be "No" of course.

Perhaps the commonest illustration concerns the prevention of the common cold by vaccine. We do not know the causative agent of the common cold and therefore the bacterial vaccine used to prevent colds does not contain it. Is it therefore necessarily illogical to give these bacterial vaccines as a preventive of colds? The answer must be that it is not necessarily illogical although there is no evidence that it is logical, because immunity to the cold may be produced by nonspecific therapy.

Among all persons wishful thinking, or the rationalization of what we desire, is common. We know what we want and therefore build up arguments in its favor.

One could give many illustrations of errors in reasoning mostly based on the fact that in the reasoning only one instead of several possibilities is considered. The type of thing to which I refer is the reasoning that in pneumonia there is usually a high fever, therefore any high fever may mean pneumonia. Of course, such an illustration seems absurd. On the other hand physicians do not hesitate to argue that, because appendicitis is often accompanied by a leukocytosis, therefore if there is any leukocytosis the diagnosis is appendicitis.

#### UNDUE DEPENDENCE ON SEDIMENTATION TEST

Many tests have been devised merely because the advocates of these tests, finding the tests positive in some particular disease and negative in normal persons, concluded that the test was diagnostic of this disease. In many instances the test is merely positive for some general type abnormality as fever. A vast amount of literature has been accumulated on the so-called blood sedimentation rate. Following loose reasoning, the blood sedimentation rate was supposed to be diagnostic of a wide variety of conditions. It was pointed out, when the sedimentation rate was being discussed in the early stages, that in normal persons there was a normal sedimentation rate. In many, but not in all, diseases there seemed to be an alteration in the sedimentation rate. It was merely one of the many things that happen; the human organism is not normal. Changes in a sedimentation rate in the same individual may be of some value in determining the course of the disease and indeed the prognosis. After a good

many years, that is the conclusion which has emerged out of a huge mass of contradictory and conflicting conclusions and summaries. Even now undue dependence is placed on this test, in the first place because there is no specificity about this test and, in the second place, because there may be some other condition which is altering the rate besides the condition which is being studied.

#### CAREFUL DEDUCTIONS NECESSARY

In every field of medicine one could multiply the argument for the necessity of careful and thorough deductive reasoning. As I have pointed out elsewhere, the examination of the urine is not a perfect test for nephritis or diabetes. Indeed, the examination of both the blood and the urine, while giving a great deal of information, may be neither dependable nor precise. The reason for this is that the morbid processes are within the cells and the blood itself is only one step nearer the cells than is the urine. There is a good deal of evidence that the blood is used for a sewerage system and does not always reflect exactly the condition of the cell. There may be other factors which may affect the blood and urine figures. For example, a marathon runner will present a urine of acute nephritis. A starving patient will show a blood nonprotein nitrogen content which is that of uremic coma. Furthermore, if he is starving and has enough acidosis to produce a high nonprotein nitrogen level, he may also present a urinary picture of nephritis. It would be easy to multiply these casual observations in the field of medical investigation but, suffice it to say, every procedure is subject to each of the factors which have been considered.

Even if careful of our observations, our statistics and our logic, we must admit that many of the processes which we study are little understood. From time to time that will result in seeming refutation of the value of logic. The so-called Wassermann test is an adaptation of the complement fixation test. It was originally considered to be specific because, presumably, a specific antigen was used. We now know that the antigen is not specific, yet the test runs as closely to being perfectly accurate as one can expect on the law of chances. Somewhere there is a reason for it. While we accept with gratitude the extraordinary accident that has given us such a useful test as the Wassermann test, this experience is a chastening example of our fundamental ignorance and it points to the necessity of avoiding at all times a completely dogmatic point of view.

Hard, sound reasoning and logical deduction can be developed as a part of the necessary equipment of the medical investigator. They are as vital as accurate observation or adequate statistical data. Wishful thinking and rational-

ization belong to the same category of scientific sins as erroneous observations and misleading statistics. It should be and, indeed, must be the only satisfactory destiny of medicine to be the science of medicine. As such, the science of medicine will, we trust, be grouped with the physical sciences and the natural sciences. We like to think that we are close kin to these somewhat rigid sciences wherein data are factual and statistically adequate, and reasoning is as sound and relentless as the limitations of the present knowledge permit.

### TRENDS IN MEDICAL PRACTICE

*Abridgment of presidential address by Dr. Fred W. Rankin of Lexington, Ky., read before the Postgraduate Surgical Assembly, the ninth annual meeting of the Southeastern Surgical Congress, Louisville, Ky., March 8, 1938, and published in the Southern Surgeon, June 1938.*

The two most noticeable trends in medical practice to develop in the last quarter century are, first, specialization; the second, the injection of governmental influence, both state and federal, into control. The enormous trend toward specialization and also practice by cooperative consultation methods seems to portend that in another generation medicine may largely be practiced, in urban centers at least, around (a) medical schools and teaching hospitals, (b) nonteaching hospitals, (c) loosely associated consultation groups with a central laboratory, (d) privately owned clinic groups, (e) independent consultation and (f) general practice.

The essential changes which are now taking place and which the practice of medicine has been undergoing for a quarter of a century demand a different policy in the matter of graduate training which supplements the undergraduate course. Graduate training concerns the entire medical profession and falls readily into three groups: (1) for the specialist, (2) the research worker, and (3) that group of medical men desiring either to change from the type of general practice they are doing or who, maintaining their present type of practice, desire to keep abreast of the scientific times.

Many of the practitioners of necessity find themselves engaged in the fields of both internal medicine and surgery. This is the group which will continue to gain advantage from refresher courses of short duration in graduate institutions, by attendance on postgraduate assemblies and by extension courses under control of state medical societies. The whole plan of practice cannot be changed abruptly or completely, but provision must be made for their professional stimulation and advancement by some scheme incorporated in any broad plan of postgraduate instruction.

The research worker, on the other hand, represents but a small group of the profession. The problem of his training almost invariably is put back into undergraduate medical institutions and foundations equipped with endowments for this purpose. Lack of time or the absence of research spirit plus the urgency of changing economic relationships will decrease the number of available research men, but they should be encouraged and stimulated to further study.

Today among physicians of the United States one out of six is a full time specialist and an almost equal number may be listed as part time specialists. It is futile to deny that specialization is rapidly extending throughout the profession. Perhaps it is the result of evolution in the development of special, highly technical procedures, but there is an obligation on the profession to see that the public is protected against self-appointed and inadequately trained specialists.

The hospital is the keystone of graduate surgical teaching. Operative experience must be provided for surgeons. No graduate course however long or satisfactorily administered from the standpoint of surgical pathology and diagnosis is complete unless the candidate actually carries out the operative act in a sufficiently large number of cases to warrant receiving his preceptors' stamp of approval as an accomplished surgeon.

It is the responsibility of the profession to make these men safe by providing them adequate training. The great hospitals of the teaching centers and clinics are not sufficient in number for this purpose and consequently facilities must be sought in nonacademic hospitals conducted by proficient staffs under controlled conditions. . . .

### AMERICAN BOARD OF SURGERY

Fostered by the American Surgical Association and participated in by sectional surgical societies, the surgical section of the American Medical Association, and the American College of Surgeons, the American Board of Surgery was organized. The avowed purpose of this board is to increase the opportunities for surgical teaching and to elevate the standards of surgery. . . .

The Council on Medical Education and Hospitals of the American Medical Association has more recently launched a campaign to make a study of all phases of graduate medical education. A Commission of Graduate Medical Education, authorized by the Advisory Board of the Medical Specialties, has been created to mobilize current opinion as to how the problems in their field can best be solved and to formulate the fundamental principles involved in graduate training. . . .

These concerted programs by different national bodies show the intense interest the medical profession has in affording more opportunities to more men for training, and the desire to cooperate with one another. These authoritative bodies promise a definite plan for the future which will be practical and workable for the education of a specialist in any particular field.

#### SOCIALIZATION OF MEDICINE

The second major trend which is influencing the practice of medicine and probably will project its shadow largely into the future unless there is deviation from its apparently charted course is the attempt of the government to subsidize and control health services. Efforts of persistent, persuasive, purposeful, probably public minded, but certainly politically controlled, pressure groups to extend public health agencies and to dominate, under governmental auspices, medical service, if successful, will bring us nearer and nearer to some modified state of socialized practice. This is a menace intolerably abhorrent to the majority of practicing physicians. Bureaucratic control, whether by state or federal agencies, inevitably, if one may judge by the experiences and reports of Continental attempts at socialization of medicine, results in a lowering of the standards of professional care and obtunds the ambition and interest of the practicing physician.

It is unbelievable that socialization of medicine, as the picture is usually projected, is an immediate possibility in the United States, nor can one willingly accept the thesis that it is a necessary part of an evolutionary socio-economic scheme to which we are apparently committed. The practice of medicine in this country has rested securely in the hands of organized medicine for centuries and, while there may be justification at times to chafe at what appears to be ultraconservatism, it is well to remember that in times of change it is improbable, indeed it is foolish to assume, that any sociopolitical agencies should have at heart the improvement of the nation's health more than scientific bodies. It is equally unlikely that these groups are better able to estimate and forward any movements to improve the general status of the public's health than those whose everyday task it is.

Despite charges of proponents of radical change in medical practice there is no obstruction on the part of the organized medical profession to progress nor is there a tendency to be reactionary in method. Under no compulsion from any source, the medical profession has continued through many vicissitudes, extending back into remote ages, to follow a charted course of advancement which has resulted always in elevation of standards of education and practice in curative and preventive medi-

cine. The medical profession is continually subjecting its methods of practice to careful, painstaking and unbiased scrutiny and demanding of its adherents a higher grade of efficiency. The reduction of infant mortality, the advances in combating communicable diseases, the increase of life expectancy and the wholehearted support of the present movement within its own ranks to certain qualified specialists are samples of accomplishments which refute many of the accusations of its critics.

That the present turbulent social unrest throughout the world necessitates certain changes in medical practice is admitted by all. That governmental systems giving funds raised by taxation could be advantageously integrated with the present system of caring for the indigent and near indigent and without subsidizing the service is hardly debatable. Many arguments for cooperation and coordination of governmental agencies and the present system of practice of medicine may be advanced. However, an enormous amount of study and correlation of data must inevitably be done before a definite decision on the necessity of change of any magnitude in today's present system of practice is arrived at.

No medical man would object to changes in medical practice which were advantageous to the nation's health and which beyond cavil were not politically fostered, dominated and directed. The medical profession has no disinclination to aid and cooperate with authorities whose aim is improvement of the health of the underprivileged, but the extension of a health program which is all inclusive and controlled by federal authorities wholly or in part seems an extraordinary procedure distinctly open to question.

#### OBJECTIONS TO STATE MANAGED MEDICINE

The main objections to state-managed medicine fall into three categories: first, the huge increase in the cost of medical care; second, the decline of medical services, and, third, the abuses both political and professional which this type of service encourages. The economic considerations under even mild scrutiny indicate a great increase in the cost of medical care due to enormous administrative expenses. If one may judge by any standards of governmental control hitherto imposed, this is an inescapable conclusion.

To the second proposal that medical services depreciate under bureaucratic control, one need only point to the incontrovertible facts that mortality and morbidity are not reduced, graduate education and study decline, research languishes, and political issues become predominant and human values secondary.

A united front by organized medicine must be presented to these proponents of political

domination and agitators for cataclysmic changes in the present day type of practice. The medical profession itself has a concrete answer to socialization in the type of service it renders to the community. Its obligation is to continue to practice good medicine and to advance the cause of preventive medicine and research in the full realization that the care of the sick is the paramount duty of the doctor.

Any system which places medical service in a position to be influenced by political expediency and opportunism inevitably forces scientific bodies under the control of nonmedical agencies and defeats the professed idealism of the ambitious advocates of health control outside of professional medical organizations. With a reduced type of service, with an increased cost, with a consideration of the experience of European countries which have adopted some form of socialized medicine, all repugnant to the individualism of a true democracy, shall we not consider well before any visionary, untried schemes in this country make us deviate from the well tried methods of practice handed down to us from the pioneers of our guild?

The medical profession believes that these accomplishments should be carried out in regular and thoughtful sequence. The health of the nation is safe in the hands of the medical profession.

#### STUDENT EPHRAIM McDOWELL

The typical American story of the first ovariectomy has a prominent place in the history of medicine. The father of ovariectomy, Dr. Ephraim McDowell, was a Virginian by birth (1771) who had received the best education that the early days in America could afford. When 19 he began the study of medicine as an apprentice to a busy practitioner and after three years went to the University of Edinburgh for additional training. Returning in 1795, he began the practice of medicine at Danville, Ky., then a village of about 500 people on the frontier of the new civilization. Having recently attended one of the great medical schools and having been under the influence of famous independent teachers, notably John Bell in Scotland, McDowell was soon engaged in extensive practice and was traveling long distances from Danville by horseback. Fourteen years after he began practice he was called out 60 miles to see a Mrs. Jane Todd Crawford, who considered herself to be pregnant and had exceeded the allotted time. Dr. McDowell examined Mrs. Crawford and explained to her that she was not pregnant but was suffering from an enlarged ovary. He explained that her condition was serious and that, although he had never heard of an attempted surgical

removal, if she would come to Danville he would endeavor to remove the tumor. Mrs. Crawford was quite willing to undergo the experiment and she rode the 60 miles on horseback with her enlarged abdomen resting on the horn of the saddle. With no experienced assistants and in his own home under conditions that would shock surgeons of today, McDowell opened the abdomen and for the first time successfully removed a large ovarian cyst, including the "sack which weighed seven pounds and one half" and fifteen pounds of a "gelatinous-looking substance." Mrs. Crawford recovered and returned home by horseback in twenty-five days in good health. She died thirty-two years later at the age of 79. The house in which McDowell performed the first ovariectomy in 1809 is still in Danville, where also is a beautiful monument erected under the sponsorship of the Kentucky State Medical Association to mark McDowell's present burial place.

Little is known of McDowell's student days. Schachner's<sup>1</sup> research reveals that he was a conversationalist with ready wit and that he could sing English and Scotch songs with comic effect. He was temperate and did not use tobacco. At 31 he married the 18 year old daughter of Kentucky's first governor, and to them six children were born.

In Edinburgh McDowell became so interested in anatomy and surgery as a private pupil under the famous teacher John Bell that he was not inclined to give the university courses the attention which justified awarding a degree. Trout<sup>2</sup> writes that he was accompanied to Edinburgh by Samuel Brown, another medical student, who was a brother-in-law of McDowell's preceptor, Dr. Alexander Humphreys. In his letters Brown indicates that McDowell attracted the attention of his classmates, who selected him to defeat a boastful Irishman in a foot race of 60 yards for a stake of 10 guineas. McDowell who was of Scotch origin, purposely allowed the Irishman to win the smaller stake and then challenged him to a longer race with a stake of 100 guineas, which he easily won.

Pecuniary difficulties in his student days may have required further consideration, for his father wrote to his son-in-law as follows:

I fear that I shall not be able to give Ephraim money sufficient to take with him, if he goes to Scotland next fall. I forgot to tell Ephraim to write me as soon as possible when he is to set out for Scotland. I would be glad he did not go till September next, as by that time I may have at my power to send him some more money than I can do this spring. I have enclosed Ephraim a warrant on the treasure for sixty-five pounds and kept a duplicate of it lest it should be

1. Schachner, August: Dr. Ephraim McDowell, "Father of Ovariectomy": His Life and His Work, Bull. Johns Hopkins Hosp. 24: 153 (May) 1913.  
2. Trout, Hugh H.: The "Scotch-Irish" of the Valley of Virginia, and Their Influence on Medical Progress in America, Ann. M. Hist. 10: 71 (Jan.), 162 (March) 1938.

lost, and I hope to send him another warrant in April or May next for seventy-five pounds. Pray keep your eye on Ephraim and see how he conducts and let me know your opinion, if I might trust him with what money may be sufficient for him to Scotland.

It is unfortunate that McDowell wrote so little. His only contributions to medical literature were two papers published in 1817 and 1819 concerning his first five cases of ovariectomy. Of eight other cases which followed he wrote nothing. James K. Polk, later President of the United States, was one of McDowell's patients whom he treated for "stone" and for hernia. Although he had earned fame, it seems that he did not especially desire notoriety.

### CAN STUDENT FAILURES BE REDUCED?

Of the students who enter medical schools, from 10 to 50 per cent never graduate. It would be impressive if the effect on the personality and character of the subsequent careers of the failing students could be analyzed. While no one wishes a graduate to enter practice unless properly qualified, some doubt remains as to whether every possible expedient has been adopted to reduce failures.

The answer does not lie merely in the selection of students. The technic of selection is imperfect and will always be so. No technic dealing with people is better than the procedure in applying it, and here the human factor enters. It is desirable to improve the procedure in student selection, but it is believed that other expedients may be employed to reduce student failures. Some suggestions are offered for reducing student failures.

At the Medical College of Virginia, first year students in the medical school were requested last fall to report two weeks earlier than students in the upper classes. During this extra time the regular class schedules operate, although the amount of work assigned daily at first is somewhat less than has been assigned to freshmen in previous years. It is thought that beginning the year with a slow tempo will enable students to catch in time the accelerated stride expected of them more certainly, and that seems to have been the case. As yet there are no definite results from the experiment and no assurance that it will be continued indefinitely. The impression has been gained, however, that it may have value and should be continued long enough to ascertain whether that is true.

Our professor of anatomy has made another suggestion, namely that a larger group of students be admitted to the first year class and that they report two or three weeks earlier with the expectation that at the end of six or eight weeks

the class be chosen to be carried through the year. This would have the effect of turning back those students which are eliminated in time for them to enter some other course of study during the same year or take up some type of employment. The matriculation would be tentative and the sense of failure, which is a great blow to some types of personality, would be softened.

The student is not the only factor in failures. Poor teaching makes its contribution and better teaching beginning in the lower grades and continuing through high school and college might well have more consideration in professional schools.

Liberal arts faculties often do not realize what is expected of students in the medical school. It might be emphasized repeatedly to the various college associations that generally medical students are required to carry a larger volume of work with a higher degree of accuracy than the students of liberal arts colleges. Frank discussions with the deans and faculties of such colleges is likely to be the more direct method of placing this emphasis.

It has been suggested that the preparation for medicine be shortened one year and the medical course lengthened one year, the first year of the five year medical course to include the completion of premedical preparation and beginning of medical study. It is argued that the proper transition from college to medical school could be made advantageous during this period.

The fear of failure suffered by some students may be a dominant factor in their failure. Fear devastates some types of persons and the fear complex should be allayed whenever possible. The proper faculty-student relationship may contribute much to this end. Upper classmen also play a role in developing the fear complex among students of the lower classes by exaggerating the difficulties and hardships of progress through the medical course. While this is not an easy situation to deal with, it can be counteracted in part by a proper stand by the faculty.

### THE PEDAGOGIC SIN

The reduction of student failure is a complex problem. One student may be better suited in one set of circumstances and another student may be better suited in different circumstances. Teaching of a certain kind may be better for one student and may not be for another student. The pedagogic sin lies in ignoring the issue on the assumption that the trouble lies solely with the student and that the school has no responsibility in the matter.

A curriculum like medicine, which is largely prescribed, cannot take into account to an ample degree the full import of individual differences. It is too much to expect that a student will do quite as well in chemistry as in anatomy, or

vice versa. In dealing with students one must keep constantly in mind the principle of individual differences; otherwise, injustices will be committed.

It would be difficult to segregate preventable from inevitable failures. The author's effort here has been simply to state the problem and to express the belief that something can be done to solve it in part; something definitely constructive must be ever pursued, always with an experimental attitude.

### THE GENERAL PRACTITIONER AND NATIONAL PHYSICAL FITNESS

In a symposium on the National Campaign for Physical Fitness in England, the role of the general practitioner was discussed by W. W. Forsyth, M.B.<sup>1</sup> The general practitioner, he said, has little influence on the well being of the individual in early life because this care has been taken over by the public health officer, who also claims the postnatal, preschool and school years. The public health officer also claims the individual's infectious illnesses and a main part in his vaccinations and immunizations. Only when the individual becomes a fledgling, Dr. Forsyth said, does the family physician get a chance. There remain, then, three lines of activity for the general practitioner. The first is instruction in measures for maintenance of health. The public has a colossal appetite for matters pertaining to health and the general practitioner, with his wide experience of people, fads and circumstances, is best fitted to give unbiased opinions on the value of health measures.

The most valuable contribution the general practitioner can make in safeguarding health is by conscientiously caring for the sick. In so doing he plays the greatest role in the maintenance and restoration of health. Does he not guard the patient against complications and impress on him rules of health applicable to his case? He advises people how to maintain their health and encourages them to be examined as soon as they feel that there is anything wrong. If he had a larger share in the public health services he would do more in the way of prevention; but that line of approach is often closed to him. He is the backbone of the staffs of the smaller hospitals throughout the country, as well as in numerous other institutions where love of his work is his only reward.

The first thing the general practitioner asks of you is loyalty in telling him your symptoms early and fully; loyalty in believing his opinion when it does not happen to fit with your own; loyalty to his treatment even when it does not meet with your neighbor's idea as to what he

ought to do; loyalty in not forsaking him because a neighbor persuades you that another doctor would know better how to deal with your case. I know a man, said Dr. Forsyth, who walked through several streets with a bandage on his neck on his way to the doctor. He met several inquiring friends and arrived at the doctor's office with nine different cures for boils. And it was not a boil that he had after all.

The health services will be all the better for more cooperation with the general practitioner. It is nonsense to give as an excuse that he is not sufficiently trained in preventive medicine. He is among the few citizens who are in the position of being able to appraise public health measures. He is not likely to give his whole hearted support to what may be called the recreational type of health activity, of which the "keep-fit classes" are an example. He feels that the first essential of exercise is the open air. He will give all his support to the development of playing fields and more open spaces, and to physical contests.

The general practitioner would teach the public to avoid fads and face rather than fear symptoms. As family physician he is an indispensable instrument of national health policy, and without his assistance as health adviser and as a principal liaison between the homes of people and the statutory medical services, these services cannot function to the maximum in a comprehensive policy for promoting the health of the people. Dr. Forsyth closed his discourse with the words of an important and unbiased committee:

We regard it as of primary importance that the organization of the health services of the nation should be based upon the family as the normal unit and on the family doctor as the normal medical attendant and guardian. It is not for disease that provision has to be made, but for persons liable to or suffering from disease. The first essential for the proper and efficient treatment of individual persons is therefore not institutional but personal service, such as can be rendered to people in their own homes, only by a family doctor who has the continual care of their health; to whom they will naturally turn for advice and help in all matters pertaining thereto; who will afford them such professional services as he can render personally; and who will make it his duty to see that they obtain full advantage of all the further auxiliary services that may be otherwise provided.

**Mental Defectives and Epileptics.**—Ninety-five per cent of all mental defectives and epileptics in the United States receiving institutional care were found in state institutions, according to the Bureau of Census figures for 1936. About 4 per cent of these patients were in private institutions and 1 per cent in city-owned institutions. A much higher percentage of epileptics died in institutions during that year than did mental defectives. *Public Health Reports*, May 27, 1938, states that at the end of 1936 there were 114,574 such patients in institutions throughout the country. This number does not give even an approximate measure of the total number in the country, since many are at large or in prisons, reformatories, alms houses and hospitals for mental disease.

1. Forsyth, W. W.: The Role of the General Practitioner, J. Roy. San. Inst. 58:546 (May) 1938.



## Medical College News

*Medical schools, hospitals and individuals will confer a favor by sending to these headquarters original contributions, reviews and news items to be considered for publication in the Student Section.*

### Annual Meeting of Association of Medical Students

The Association of Medical Students will hold its annual meeting in Philadelphia, December 28-30, with the five medical schools in the city acting as hosts. The convention headquarters will be at the Hotel Philadelphia, Thirty-Ninth and Chestnut streets. There will be clinics, demonstrations and lectures at all the medical schools, and scientific exhibits, including the exhibit on "Cardiovascular-Renal Disease, Clinical and Pathologic Correlation," which was awarded a gold medal at the annual session of the American Medical Association in San Francisco last June. There will also be commercial exhibits, hobby exhibits, motion picture demonstrations, including "Artificial Circulation with Survival of the Animal" and "Delivery of Triplets," a convention dance Thursday evening, and a banquet Friday evening, at which Dr. R. G. Leland, director of the Bureau of Medical Economics of the American Medical Association, and Dr. James H. Means, professor of medicine, Harvard Medical School, will discuss "Trends in the Distribution of Medical Care."

The registration fee for the convention is \$7, which includes two nights at the hotel, the banquet, the luncheon, the dance, and transportation to the medical schools to attend the lectures and demonstrations. The registration fee for those not stopping at the hotel will be \$3.50. Furthermore, each delegate to the convention will receive, without charge, a copy of the convention book containing articles by well known physicians, the annual committee reports, and other material.

The theme of the 1938 convention is "Preventive Medicine."

The tentative program is in part as follows:

### WEDNESDAY, DECEMBER 28

8-10 a. m.—Registration.

10 a. m.-12:45 p. m.—Lectures, demonstrations and clinics at University of Pennsylvania.

Dr. O. H. Perry Pepper, professor of medicine, "Preventive Phases of Internal Medicine."

Dr. Eldridge Eliason, professor of surgery.

Dr. A. N. Richards, professor of pharmacology, "Renal Physiology."

Dr. David Drabkin, assistant professor of physiologic chemistry, "Spectroscopic Studies of Pigment Metabolism."

Dr. Eliot R. Clark, professor of anatomy, "Development of Blood and Vascular Channels in the Rabbit's Ear" (motion pictures).

1 p. m.—Luncheon, Hotel Philadelphian.

Address of Welcome: Dean William Pepper, University of Pennsylvania School of Medicine.

Address: Dr. R. R. Spencer, senior surgeon, U. S. Public Health Service, "Preventive Medicine."

3-5 p. m.—Discussions.

7:30 p. m.—at Hotel Philadelphian:

Motion Pictures: "Delivery of Triplets."

"Artificial Circulation with Survival of the Animal."

Student scientific papers.

### THURSDAY, DECEMBER 29

10 a. m.-2 p. m.—at Woman's Medical College:

Dr. Catherine Macfarlane, professor of gynecology, "Prevention of Carcinoma of the Cervix."

Dr. Helen Ingleby, professor of pathology, "Breast Tumors." Ben King Harned, Ph.D., professor of pharmacology, "Eugenic Aspect of Diabetes in Rats."

10 a. m.—at Temple University School of Medicine:

Dr. W. Wayne Babcock, professor of surgery, "The Surgical Aspects of Disease of the Thyroid Gland."

12:30 p. m.—Dr. John A. Kolmer, professor of medicine, "The Present Status of Methods of Preventing Acute Anterior Poliomyelitis."

Demonstration in the Bronchoscopic Clinic, Drs. Chevalier Jackson and Chevalier L. Jackson in charge.

Recent Studies in Neurology. Drs. Walter I. Lillie, Temple Fay and Michael Scott (motion pictures).

At Hahnemann Medical College:

Clinics:

9-12 a. m.—General surgery, Dr. William M. Sylvius.

2-7 p. m.—Orthopedics, Dr. John A. Brooke.

7 a. m.-noon.—Gynecology, Dr. E. B. Craig.

12:30-5 p. m.—Nose and throat, Dr. C. B. Hollis.

Exhibits at Hahnemann Medical College:

I. Cardiovascular-Renal Disease. Drs. Frank W. Konzelmann, Edward Weiss, Lawrence W. Smith, Walter I. Lillie and Edwin S. Gault.

II. Neurophysical demonstration of spatial brain lesions, Drs. E. H. Dickinson, J. S. Lehman, H. R. Fisher and H. J. Rickard.

III. Diseases of the chest, Dr. J. W. Frank, clinical chief of x-rays and Dr. J. Antrim Crellin, clinical chief of outpatient chest clinic.

9 p. m.-1 a. m.—Convention dance.

### FRIDAY, DECEMBER 30

10 a. m.—at Hotel Philadelphian.

Business Meeting. Reports of officers and committees. Election of officers.

7 p. m.—Banquet.

### The Appointment of Interns in New York

Regulations to safeguard the merit system in the appointment of the nearly 800 interns that serve the New York City municipal hospitals have been announced by the commissioner of hospitals, Dr. S. S. Goldwater. Heretofore the medical boards of the individual hospitals have determined their own procedures in the selection of interns and some of the boards have not conducted written examinations while others have. The new regulations require that the medical boards adhere to certain basic requirements in procedure that will be uniform for all the hospitals with slight modifications to permit a reasonable degree of flexibility for certain hospitals with special clinical makeups. In rating the interns, preliminary education and scholastic records will rate 30 per cent, written examinations held under identification by numbers and without knowledge of the name 30 per cent, and rating based on oral examination 40 per cent. The appointment of successful candidates is a charter function of the commissioner of hospitals and will be based on the results obtained under the three sections of the examination.

### Dr. John W. Spies Appointed Dean at Texas

The Board of Regents of the University of Texas has appointed Dr. John W. Spies as dean of the medical school at Galveston and professor of public health. Dr. Spies was born in Texas, graduated from Harvard University School of Medicine in 1924 and received the degree of master of science from Yale University School of Medicine in 1930. He interned at St. Luke's Hospital, New York, served a residency and clinical fellowship at Memorial Hospital, New York, and served fellowships at the University of Louvain. He was formerly instructor in surgery and pathology at Yale University School of Medicine and associate professor of surgery at Peiping Union Medical College, China. From 1935 to 1938 he was director of a hospital in Bombay, India. He has the certificate of the National Board of Medical Examiners. He is the brother of Dr. Tom D. Spies, professor of medicine at the University of Cincinnati, who has recently reported research on the treatment of pellagra, particularly with nicotinic acid.

### Louisiana Personal

Dr. William B. Clark, New Orleans, was recently made associate professor of ophthalmology at Tulane University School of Medicine, and placed in charge of the eye department of the Hutchinson Memorial Clinic and of graduate instruction in ophthalmology at the Eye, Ear, Nose and Throat Hospital.

### Student Distinguished Service Award

The faculty of Wayne University College of Medicine, Detroit, has established a distinguished service student award to be made to the senior student who during his four years in the college of medicine has rendered noteworthy service to the student body and faculty in promoting the welfare of the college and the university. For 1938 the award, which is in the form of a watch-charm emblem, went to Harold Longyear, who is now interning at Grace Hospital. The Alumni Association of Wayne University College of Medicine each year gives an award of \$50 to the student who has the highest scholastic standing for his four years of medical study, and this award in 1938 went to Aldred Bleier, now interning at Receiving Hospital.

### National Board Questions in Anatomy

Following are the questions used by the National Board of Medical Examiners in anatomy in part one of the examination, held September 12-14:

Answer any five questions. 1. Locate (a) the subcutaneous or external inguinal ring, (b) the abdominal or internal inguinal ring, (c) the femoral ring. Give in each case the boundaries of the ring, important relations, and the structures it transmits. 2. Discuss the histology of the different ways by which bone can grow. 3. Give the exact position of the sympathetic trunk (lumbar ganglionated chain) in the abdomen. From what sources does it receive preganglionic (activating) fibers and what branches does it give off? 4. Describe the embryonic development of the upper jaw and give all the deformities which may occur in its development. 5. Give the origin and complete course of the main arterial trunks supplying the brain as a whole. Describe their terminal anastomosis. 6. In what localized regions and parts of the body is fat commonly stored and for what general purposes? What regions show the loss most, and what regions least? Mention two regions where fat is not found.

### Michigan Personals

In October the executive staff of the University Hospital, Ann Arbor, appointed Dr. Cyrus C. Sturgis as chairman of the committee on interns.—Charles Brandman, Toledo, Ohio, a member of the junior class of the University of Michigan Medical School, was killed in an automobile accident in Toledo, September 30.—Dr. Joseph W. Nadal, a 1937 graduate of Harvard University Medical School, has joined the staff of the department of surgery at the University Hospital, Ann Arbor, and will serve as research assistant during the coming year. Dr. Nadal interned last year in the Geisinger Memorial Hospital, Danville, Pa.—Dr. John M. Dorsey, associate professor of psychiatry, University of Michigan Medical School, has resigned to engage in private practice in Detroit; he will also be psychiatric consultant to the Children's Center maintained by the Children's Fund of Michigan.

### The Annual Blockley Dinner

The fifty-second annual dinner of the Association of ex-Resident and Resident physicians of the Philadelphia General Hospital was held December 6 at the Bellevue-Stratford Hotel, Philadelphia. Dr. Randle C. Rosenberger, professor of preventive medicine and bacteriology at Jefferson Medical College, Philadelphia, was the guest of honor. Dr. Rosenberger, who graduated from Jefferson Medical College in 1894, was assistant pathologist at old Blockley in 1898 and director of the laboratory there from 1903 to 1919. Among the guests of the association were Dr. William C. Hunsicker, director of public health for the city of Philadelphia, Judge Harry S. McDevitt, Dr. William G. Turnbull, superintendent of the Philadelphia General Hospital, and Dr. Robert C. McElroy, president of the Blockley Medical Society. Dr. John J. Dailey, who is president of the association this year, was toastmaster.

### Founders' Day at Medical College of Virginia

The Medical College of Virginia, Richmond, celebrated Founders' Day December 1, marking the hundred and first anniversary. Mr. Virginus Dabney, editor of the Richmond *Times-Dispatch*, spoke on "Medicine in a Changing World." The exercises were preceded by a procession of visitors, the faculty and members of the student body.

### Health Examination of Students at Michigan

For the last four years all students entering the University of Michigan Medical School have been given a routine x-ray examination of the chest, and for the last two years all students enrolled in the medical school have been given annual physical examinations. The incidence of active pulmonary tuberculosis found among 2,342 male students examined in 1938 was 0.38 per cent, while among 1,022 female students examined the incidence was 0. This is in contrast to a rate of 0.74 per cent of active tuberculosis found among male students in 1935 and 0.87 per cent found among female students in that year.

### California Personal

Dr. Langley Porter, dean of University of California Medical School, is visiting medical schools of universities of the United States and Canada, during which time Chauncey Leake, Ph.D., professor of pharmacology, is acting dean.

### The Jones Lectures at Oregon

Dr. Arno B. Luckhardt, professor of physiology at the University of Chicago, gave the annual N. W. Jones lectures November 2-4 at the University of Oregon Medical School, Portland. His subjects were "Dr. William Beaumont and the Beaumont Memorabilia of the University of Chicago," "Academic or Unsuccessful Research" and "A Neglected Chapter in Anatomic Illustration and Instruction."

### Connecticut Personal

Ira V. Hiscock, professor of public health in the Yale University School of Medicine, New Haven, Conn., has been elected president of the National Health Council for 1938.

### Appointments at Harvard

The following appointments have been announced by Harvard University, Boston, for one year from September 1:

- Dr. Augustine Thornton Scott, Lexington, Mass., assistant in medicine.
- Dr. William F. Orr Jr., Nashville, Tenn., assistant in neurology.
- Joseph Shack, Mattapan, Mass., assistant in physical chemistry.
- Heron O. Singher, Red Hook, N. Y., assistant in physical chemistry.
- Dr. Thomas W. Botsford, Chillicothe, Mo., assistant in surgery.
- Timothy J. Kurotchkin, Peiping, China, research associate in bacteriology and immunology.
- Ernst T. von Brucke, Innsbruck, Germany, research associate in physiology.
- Dr. John H. Venable, assistant professor of anatomy at Emory University, research fellow in anatomy.
- Dr. Jonathan F. Meakins, Montreal, Canada, research fellow in bacteriology.
- Dr. William E. Smith, Baltimore, research fellow in bacteriology.
- Willy K. Rieben, Berne, Switzerland, research fellow in biologic chemistry.
- Dr. John Romano, Milwaukee, research fellow in neurology.
- Haim Haimovici, Rumania, research fellow in physiology.
- Per O. Therman, Helsingfors, Finland, research fellow in physiology.
- Dr. Albert Y. Kevorkian, Chestnut Hill, Mass., research fellow in surgery.
- Dr. Nathan Rudo, Baltimore, research fellow in pathology (Oct. 1, 1938, to Sept. 1, 1939).
- Dr. Richard G. Horswell, Chicago, research fellow in medicine (Jan. 1, 1939, to Sept. 1, 1939).

**Son Succeeds Father in Orthopedic Department**

Dr. Joseph A. Freiberg, associate professor of orthopedic surgery, will succeed his father, Dr. Albert H. Freiberg, as head of the department of orthopedic surgery of the University of Cincinnati College of Medicine. The elder Dr. Freiberg resigned in July after forty years of service. Since then his son has been acting head.

**Temple Establishes Four Year Course for Technicians**

Temple University has established a four year course in medical technology leading to the degree of bachelor of science in medical technology. The work of the first two years is taken in the college of liberal arts and sciences and the last two in the medical school and Temple University Hospital.

**New Department in Public Health at Loyola**

A new department offering courses leading to the master's degree in public health for graduate students, the certificate and bachelor of science degree in public health nursing, courses in preventive medicine for medical students and advanced bacteriology, has been established at Loyola University School of Medicine, Chicago. It is designed to attract sanitarians, public health nurses and health officers. Dr. Earl E. Kleinschmidt is in charge of the new department.

**Philadelphia Personal**

Dr. James Reid Martin, assistant professor of orthopedic surgery, Jefferson Medical College, Philadelphia, has been appointed chief surgeon at the State Hospital for Crippled Children, Elizabethtown.

**Promotions and Appointments at Georgia**

The following promotions and appointments at the University of Georgia School of Medicine, Augusta, for the session 1938-1939 have been announced:

**Promotions:**

Dr. Frederick A. Mettler to professor of gross anatomy.  
Dr. Edward S. Cardwell Jr., to assistant professor of pathology.  
Robert B. Dienst, Ph.D., to associate professor of bacteriology and public health.  
Dr. Hervey M. Cleckley to professor of psychiatry.  
Dr. Meinhard Robinow to instructor in pediatrics.  
Dr. John H. Sherman to professor of surgery.  
Dr. Richard F. Slaughter to professor of neurosurgery.  
Dr. Lucius N. Todd to professor of tuberculosis.  
Dr. Perry P. Volpito to professor of anesthesia.  
Dr. Richard B. Weeks to assistant professor of clinical surgery.

**Appointments:**

Dr. Solomon Tanenbaum to assistant in clinical medicine.  
Cecilia C. Mettler, Ph.D., to instructor in medical history.

**International College of Anesthetists Awards Medal**

Francis M. Whitacre, Ph.D., assistant professor of organic chemistry at Case School of Applied Science, Cleveland, was awarded the medal of the International College of Anesthetists at the annual meeting in New York, October 19. The award, which was made in recognition of his work on the chemical structure of anesthetics, consisted of a medal and a certificate naming Dr. Whitacre as a specialist in anesthesia and a fellow in the International College of Anesthetists.

**Puerto Rico Personal**

Dr. Roman Kenk, professor of zoology at the University of Ljubljana, Yugoslavia, has been appointed associate professor in the department of biology of the University of Puerto Rico.

**University of Cincinnati**

Dr. Max M. Zinniger recently resigned as assistant dean of the University of Cincinnati College of Medicine, Cincinnati, to devote more time to surgical research. Dr. Stanley E. Dorst is now assistant dean and Dr. Sander Goodman has been appointed assistant to the dean, Dr. Alfred Friedlander. Among recent gifts to the university was one of \$27,500 given anonymously for the department of psychiatry.

**Changes at Louisiana State University**

The following appointments to the Louisiana State University School of Medicine, New Orleans, among others, have been announced:

Dr. Albert E. Casey to assistant professor of pathology and bacteriology.  
Dr. Rupert E. Arnell, senior assistant professor of obstetrics and gynecology.  
Dr. Athol S. Kenney, assistant professor of pediatrics.  
Dr. Rawley M. Penick, assistant professor of surgery.

**Promotions on the faculty include the following:**

Dr. Dan D. Baker to senior assistant professor of anatomy.  
Dr. George N. Ronstrom, assistant professor of anatomy.  
Dr. Adolphus H. Sellmann, assistant professor of anatomy.  
Dr. James L. Gouaux, assistant professor of physiology.  
Dr. Robert H. Bayley, assistant professor of medicine.  
Dr. Karl LaVon Dickens, assistant professor of medicine.

**Lectures to Students in Public Health at North Carolina**

Dr. Louis L. Williams Jr., senior surgeon, U. S. Public Health Service, lectured on malaria to the students in the division of public health at the University of North Carolina School of Medicine, Chapel Hill, N. C., October 31 and November 1. Dr. Mark V. Ziegler, senior surgeon, U. S. Public Health Service, showed moving pictures of the work of the U. S. Public Health Service to the medical school students, November 8. Mr. Leslie C. Frank, senior sanitary engineer, U. S. Public Health Service, lectured on milk, November 15.

**Programs for Interns**

The Evangelical Deaconess Hospital, Brooklyn, is holding a series of intern training programs. For the second program December 12 discussions were held on infections of the hand, psychology of bedside manner and multiple myelomas complicated by purpura haemorrhagica.—The Manhattan Eye, Ear and Throat Hospital, New York, is presenting a series of evening lectures in ophthalmology to the resident staff.

**Museum of Medical History**

Plans are under way to establish a medical history museum at the Wayne University College of Medicine, Detroit. A request has been made for books, instruments, letters, account books, manuscripts and diaries or any other material that will help make up a historical medical collection. Additional information may be obtained from Dr. William J. Stapleton Jr., associate dean and professor of jurisprudence, ethics and economics at the medical college.

**Massachusetts Personals**

Dr. Otto Kraymer, associate professor of pharmacology at Harvard University Medical School, Boston, has been appointed to the chair of pharmacology at Peiping Union Medical College, China, beginning Sept. 1, 1939.  
Frederic L. Wells, Ph.D., head psychologist of the Boston Psychopathic Hospital since 1921, has been appointed psychologist to the department of hygiene of Harvard University.

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## CONTRIBUTION OF MENTAL HYGIENE TO EDUCATION ON THE ELEMENTARY LEVEL

JAMES HOULOOSE, M.D.  
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When one looks at the history of medicine one must conclude that its growth and development have been the result of contributions from those both inside and outside its own professional family. Thus one sees the contribution of the physicist unfold for medicine the diagnostic and curative technic, the x-rays; the biologist finds and elaborates the gene; the biochemist isolates and produces the vitamin, another the hormones. The bacteriologist gives an insight into the modes and manners of an unseen microbiologic world. The psychologist portrays the motives and mechanisms of the mind. The sociologist and the anthropologist discover the purpose and plan of our complex social civilization. If one stops a moment to consider any of the other great professional fields, one sees this same variety of contributors assisting in the integration and development of each of the other sciences. To education in the last quarter century have come contributions from almost every other professional field. The engineer suggests a wholesome school environment through proper lighting, heating, ventilation and seating. The health officer regulates and controls the morbidity of the school population through testing, immunization and vaccination. The psychologist gives the technic and tools of measurement. The last to appear on the educational scene as a bearer of gifts is the mental hygienist.

The term mental hygiene has been variously defined. In this country it was revitalized about a quarter of a century ago by Adolf Meyer, who, after listening to Clifford Beers's plea for the amelioration and the prevention of mental illness, said "I would call your plan and program the mental hygiene movement." The term has grown and, because of its dynamic concept, will continue to grow. It is best defined by the words of Samuel Butler in "The Way of All Flesh":

All our life long, every day and every hour, we are engaged in the process of accommodating our changed and unchanged selves to changed and unchanged surroundings; living, in fact, is nothing else than this process of accommodation. When we fail in it a little we are stupid; when we fail flagrantly we are mad; when we suspend it temporarily we sleep; when we give up the attempt altogether we die. In quiet, uneventful lives the changes internal and external are so small that there is little or no strain in the process of fusion and accommodation; in other lives there is great strain but there is also great fusing and accommodating power; in others, great strain with little

accommodating power. A life will be successful or not, according as the power of accommodation is equal to or unequal to the strain of fusing and adjusting internal and external changes.

Samuel Butler anticipated the concepts, point of view and philosophy of the psychobiology of Adolf Meyer.

Mental hygiene brings to education certain dynamic drives. Among the first of these drives is the movement for a change in the curriculum of the elementary school which considers the school period of the child's life as living instead of a preparation for living. The psychologists prepared the field by their intensive study of tests and measurements which brought out the fact of individual differences, abilities and learning rates. The pediatrician, with the endocrinologist, clearly established individual differences as regards physiologic and chronologic maturation levels. The sociologist pointed to the school as one of the primary social institutions which, like the home and the neighborhood, influenced, stimulated or thwarted the child. The mental hygienist now contends that these various contributions should be fused by the school, through its changing curriculum, that these result in a total integrated personality. These curricular changes are seen on every hand, beginning with the nursery and kindergarten and extending into the university level. The new curriculum bases its program on the needs, interest and motives of the growing individual rather than on reward, marks and grade placement. This "freedom to develop normally" in the new curriculum does not imply lack of discipline or guidance; on the contrary, it leads to healthy inhibitions, controlled growth and creative enterprise.

The mental hygienist points out to the educator that the school is a social environment. He contends that this environment has its effect on the growing individuals within its four walls. He argues with Herbert Spencer that "life is the adjustment of inner to outer relations" and with Louis A. Lurie that "this constant adjustment and readjustment is the process of living." Dr. Lurie continues:

Life expresses itself in conduct or behavior; hence, if one is to understand human behavior either in its normal or its abnormal phases, one must study in detail both the individual and his environment. Furthermore, it must be realized that man is more than a biologic organism; he is also a social being, growing and adapting himself to a specific environment. Hence, fully to understand human behavior one must study the individual as a psychophysical organism that is attempting to adjust to a specific environment.

Because of this potentiality, the mental hygienist demands a wholesome school environment. He urges communicable disease control and prevention in order that morbidity may take a holiday. He advocates reduction of academic failure by approaching the problem of reading with "reading readiness tests." To him, the

factor of seeing is a combination of visual acuity and proper lighting. That these essential factors are still neglected by the average educator is apparent from such researches as those of the Bureau of Nutrition and Health Education of the University of Texas on eye health. This indicated that in a total of 203 classrooms studied with the sightmeter on clear days approximately one half of the working points on both reading and writing material was subminimal (less than eight foot-candles). On cloudy days about two thirds of the working points investigated were subminimal. On cloudy days when all available light was used, about four tenths of the working points were below eight foot-candles. A cursory review of the study by the Metropolitan Life Insurance Company on "Hand-Washing Facilities in Schools" indicates that there is a great facility-lag between adequate environmental opportunity and health instruction. This is true of toilet as well as of handwashing and drinking facilities. Seating is still in most school rooms a formal-factory-screwed-to-the-floor, faulty posture producing, fatiguing and torturing affair. For years Bennet in his book "School Seating" and more recently Rowell and Henderson in "Good Eyes for Life" have renewed the plea for adequate seating. Rosenson, writing in the *New York State Journal of Medicine* as late as Jan. 1, 1938, has called attention to practices in the New York City public schools, which no doubt can be duplicated in many other places, which are a menace to both mental and physical health of children. He enumerates these unhygienic conditions as "short lunch periods, the over-emphasis on attendance records, insanitary conditions, excessive homework, overcrowded classes, and an insufficient knowledge and practice of the mental hygiene approach to children's problems on the part of teachers." Commenting editorially on Rosenson's report, the editor of the *Journal of School Health* quite deliberately asks "What shall it profit a child if he gain the whole curriculum and lose his health?"

The school environment, because of many contributions to the development of the personality, should be wholesome. The keynote to the adequate environment within the schoolroom and school situation is the teacher. As a parent substitute, as an interpreter and integrator of the social milieu, the teacher has a commanding position. This position places on her a responsibility which the National Education Association is now challenging by the searching question of Are you "fit to teach"? The school environment produces psychologic, sociologic, emotional as well as physical factors that play their role on the totality of the growing personality. On every hand one sees the school child who presents problems in behavior because of the suppressions, frustrations, rejections, identifications, feelings of hostility, inferiority or superiority produced within the school environment. If one reads Healy and Bronner's "New Light on Delinquency," Sullenger's "Social Determinants of Delinquency" and Shaw's "Delinquency Areas," one's only conclusion can be that the psychic-social-emotional environment of the school is still far from the ideal.

The mental hygienist as the preventive team mate of psychiatry brings to the school an insight into the dynamics of individual behavior. He sees all behavior as purposeful. He views the behavior of the unadjusted, the asocial and the delinquent as symptomatic of urges, drives and impulses directed into channels disadvantageous yet often satisfying to the individual.

The unadjusted teacher may bring such uncommon sense to the classroom situation that her own psychoneurotic tendencies are superimposed on her pupils. They, in turn, become the medium into which the obsessions, the phobias, the paranoid and the psychotic tendencies are liquidated. Too frequently, as indicated by Wickman's studies as presented in "Children's Behavior and Teachers' Attitudes" do teachers respond to the misbehavior of pupils as a frustration of their own personal authority. As a rule, if the behavior is positive the teacher reacts by a positive counterattack. If the misbehavior is passive or negative her response is modified by the sympathy and protective feelings aroused through the dependence and inadequacy of the pupil. In either case the punishment is for the purpose of restoring the equilibrium of the teacher. Thus resentments, emotional and educational conditioning, patterns of behavior and attitudes are formulated and fixed.

The very competitive system of the average school places a premium on speed, the acquisition of certain skills and dexterity, which has been based on chronologic age and grade level rather than on the psychobiologic maturation of the individual. Orton, in his book "Reading, Writing and Speech Problems in Children," clearly points out that disorders in these fundamental tools of learning are developmental in nature and based, as he believes, on the phenomena of unilateral cerebral dominance. Speed, competition and the grade system make of these individuals misfits who, because of organic disabilities, are left behind in the process and join the small army of those who fail and fail. The disastrous effects of failure produce, as a rule, such disrespect for the self that desire and effort are abandoned. There need be no complete failure if the individual is thoroughly understood and this understanding is made the basis for a planned curriculum.

Two mental hygiene technics have for some time been available to the school. These are the visiting teacher and the child guidance clinic services. The visiting teacher service was first introduced in the public schools some twenty years ago. This service combines the professionally trained social worker and the educator. The service interprets the child to the school and the school to the home. In many of our better school systems the visiting teacher is displacing the truant and attendance officer. The visiting teacher is constantly approaching the child who is out of school, who is failing or who is otherwise unadjusted, from the causal front. She is interested in the why and seeks the cause not alone in the child but in the school, the home and the community as well. Through such service, schools are building up a greater child centered interest, program and curriculum.

The second service is that of the child guidance clinic, a service which makes a complete sociologic, psychologic, physical and psychiatric study of its clients who are referred. This service is the direct result of an understanding of the causative factors of adult crime. These factors have led the various leaders to conclude that prevention is the only way to stem the increasing tide of delinquency and crime. Today there are some 300 child guidance clinics in operation in the United States. Some of these are attached to juvenile courts, to community social agencies and to schools.

The mental hygiene contributions to education are primarily preventive in nature. They strive to make

education more and more successful. They aim at an integration of the community resources for the development of an enlightened, intelligent, worthy citizenship.

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#### ABSTRACT OF DISCUSSION

DR. FRANK E. SAWYER, Oakland, Calif.: There are several points in Dr. Houloose's paper which warrant more consideration as to the unbalancing of school children. I refer to the sudden induction into a new and strange environment, the general problem of adjustment from then on, both in and out of school, the competitive system, the pupils who fail and fail and fail, and the inadequacy of most schools with regard to the handling of these children; and, lastly, the insufficient knowledge and practice of the mental hygiene approach to children's problems on the part of the teacher. In Oakland we don't speak of mental hygiene. We speak of individual guidance, and it starts with the teacher and the nurse, and then the school physician, who has had extensive experience in pediatrics, the attendance officer, the psychologists, and the coordinator who brings all of these people together and brings the results of their work together. Finally, there is the assistant superintendent in guidance. Now, we don't claim that this is the best system, but we find that our teachers are getting education in this subject, that they are more alert and more aware as to the problems that are causing trouble with the children. A good many of these problems are comparatively trivial. Ordinarily they might not be thought of, but they are problems that may lead to delinquency. It seems to me that from a practical standpoint there are certain things we need with regard to mental hygiene or individual guidance, in the public school system; one is the selection of teachers who have personality which enables them to deal properly with children and the second is proper education of these teachers; a third is the carrying of education into the homes.

#### SOME PHYSIOLOGIC CONCEPTS IN MENTAL HYGIENE

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LOS ANGELES

Mental hygiene stresses the integration of the person—body, mind, environment. It draws where it will and can for its bases. We who are medically oriented naturally turn to concepts not too unfamiliar in our background, trying always to coalesce them with other concepts coming from other fields, such as psychology, psychoanalysis, sociology, economics. None of us can avoid bias and none of us can see the person wholly either analyzed or synthesized—the parts working harmoniously as an integrated whole. So we find ourselves channeling in our reading and in our experience certain ways of grasping the meaning of the behavior we study—channels that we know are not wholly valid because they need yet more integration with others, but nevertheless channels that serve us as routes toward a more workable dealing with the problems before us.

In this sense I have appropriated and developed within my thinking certain concepts, mainly based on the physiologic level of the organism, which are to me helpful and indeed so essential to my thinking about cases as to be indispensable. They are derived from many sources—the work of Meyer, Cannon, Crile, Kempf, Jelliffe, Myerson, Cobb and others. I may have taken undue liberties with them, but my conscience is clear in the sense that each of us does and must appropriate from where we can those interpretations

and researches that are to us most usable and, while making acknowledgment with respect, yet know that no one of them can be responsible for their utilization by others. If I appear dogmatic, kindly credit time and language deficits that render desirable qualifications impossible.

First among these concepts I would place the idea that the vegetative nervous system, its related glands of internal secretion and its master zone—the hypothalamic region—give a physiologic underpinning to psychologic ways of viewing behavior. In the states of tonus of the viscera reside much of what we commonly think of as emotion. Through the medium of this nervous organization is accomplished that intimate interplay of activities that is, so far as we know, our instinctive, emotional and behavior life. We have passed beyond the stage of intense arguing as to whether a particular symptom, body or mental, is organic or psychogenic, because we can no longer conceive of any effect on the visceral and vegetative life of the organism that is not in some way reflecting itself in the emotion and behavior of the same organism. Conversely, likewise we do not know how a so-called emotional impulse translates itself into a stimulus susceptible of transmission along vegetative nerves, but that it does so seems beyond dispute.

Now couple with this situation the facts relative to the hypothalamic-pituitary area that have come to light in the past two decades. By the clinical experiments of encephalitis, of Parkinson's disease and of vascular disturbances in the thalamic area, as well as by planned physiologic experimentation, it has been pretty well evidenced that here is an area of nervous and glandular tissue in which organism reactions characterized as emotional seem to be focalized. I do not try to state that specific emotions are localized here—that is too naive a view. But that those reactions most intimately associated with behavior determination seem to focalize there is apparently valid. It is perhaps not essentially different from our consideration of voluntary motor activities as focalized through the prerolandic brain area; that is, while admitting that integrated working of all parts of the neuromuscular chain must be a fact for effective voluntary motor function, yet it is also true that in a peculiar way the cells of the motor cortex center or focalize these functions.

When a child is exposed to a severe stimulus such as a virus or an injury that localizes in this hypothalamic area, we accept the picture as one wherein certain centers particularly related to his daily conduct are damaged. We feel we "understand" how it is that he is the way he is and how he became that way. We may be unable to do much about it specifically, but our understanding has helped us plan a regimen and furthermore has helped us to an acceptance of the reactions. This understanding is in itself therapeutic. In much the same way, we may fairly predicate that a child exposed for years to an influence less bacterial or chemical, it is true, but one capable of modifying the neural centers and connections of this region, may have as truly organic alterations at the root of his behavior as do the others. It will not be as obvious and, having occurred over so long a time, may well be unascertainable by the methods of gross pathology. But if it is true that emotional stimuli may accentuate stomach, cardiac or thyroid conditions, and so on, it is not a far cry to seeing that all these varied disturbances may have as their common denominator an impinging on the



zones in the nervous system susceptible to this kind of influences. As I see it, then, a child may be as truly physiologically (organically) modified by rejection, fear, affection and the like acting on him as he is by more accepted types of physical stimuli. Because so many of these stimuli act on him when his conscious, reasoned, cortical components of neural action are relatively undeveloped, we have a physiologic understanding of the long accepted fact that early life is important in a behavior determining way. As he grows older, more and more his intellectual functions take a part in his life, but these are always based on, or overlying, the earlier emotionally focused functions which were once quite supreme. Too often the physician, as well as the parent and teacher, tends to forget this fact and hence fails to direct his management at levels that are appropriate to the origin of the difficulty.

I am aware of the inveterate tendency to see in the specific case validation of theories. I do not see how one can wholly escape this, because without a conceptual basis for examination observations have no meaning and, once one has a conceptual basis, meaning may be read into observations in excess of what properly inhere. But this is as may be. Certain I am that in daily experience with behavior problems of children, and in relation to their parents, I see these principles of the oneness of the psychology and physiology of the organism amply illustrated. We see spoiled children, or rejected ones, and their patterns of observed behavior are as clearcut as in more infectious types of preceding experience. I do not see how it makes workable sense without some realization that the protoplasm of the organism with its self-defending and self-righting propensities so adapts itself to the problems it faces as to work through them somehow. In so doing it often shows, not as disease processes, but as the manifestation of the adjusting processes themselves, certain behavior that must be regarded as undesirable. So jealousy of younger members of the fraternity, negativism, pugnacity, stealing—to select a random few—are not diseases per se but are symptomatic presentations of the attempts at adaptation occurring on a physiologic and psychologic basis. This is no different fundamentally than our earlier arrived at conclusion that hemorrhage and fever are but observable signs of adaptation—often distressing to the individual and for society—but biologically no different than more accepted responses of kindness, thought for others, or the secretion of gastric juice to digest the stomach contents.

Looked at this way, one no longer seeks for a specific treatment of what are only symptoms and, at that, symptoms which, given the existing conditions, probably should not be other than what they are. One now sees them as responses of an organism that has elaborated abilities to deal with facts on levels we designate as physical (organic), psychologic (intellectual), emotional (behavior), moral (social and ethical). These levels are practicable abstractions, but they really are abstractions, for the organism does not deal successively with one and then another but approaches all at once and succeeds in such parts as he can. Then we, with our aforementioned tendency to confuse analyzed parts for realities of a functioning organism, find ourselves thinking as though organic and emotional experiences were quite separate and apart. They are not, and as we have come to live ourselves into the realization of the fact that these divisions are arbitrary we have seen

somewhat better why it is that many children respond with better behavior to physical treatment and that others respond with improved physique to emotional "detensionings" in the family or school.

Furthermore, I want to stress that this physiologic series of concepts enable one to grasp the meaning of what happens in many treatment situations. We have long laughed somewhat ruefully over how little connection there seemed to be between scientific background and therapeutic accomplishment in psychologic endeavors with people. We have all had to admit that our brethren of the "therapeutic fringe" often accomplished "cures" that better trained psychiatrists did not accomplish. We have all seen and heard the interpretations by various schools of psychologic thought and listened to honest recitals of case cures to prove the interpretation. Gradually some of us have come to the conclusion that the interpretation mattered much less than the experience itself and that oftentimes states of visceral rapport are set up that have very little to do with soundness of explanation. As I now see it, something happens in the way one set of visceral-thalamic-personality organizations meets and responds to another. This is not describable in chemical or neuronc terms, but at least we now have appreciation that in the organization of the person's vegetative and affective states lies much of the ground work on which result depends.

It likewise seems to me that these concepts of the physiologic basis of behavior are helpful in removing certain psychologic concepts from the realm of mystery or vagueness. So long as "the unconscious" was only psychologically considered it had uncertainty for me; when I commenced to realize that in the vegetative functioning of my organs were excellent examples of *unconscious and yet intelligent behavior*, it began to illumine much that had before been dark. That a child behaves importantly and behaves unconsciously has been known for a long time; that this varied only imperceptibly from his later more conscious intelligent behavior gradually has been borne in on us. Whether his early behavior stems from primitive sexual or ego urges matters less than whether it is to be envisioned as strictly organic and strictly psychologic, or rather as continual meeting of the needs of life by incorporating material from the world about, reshaping those needs in relation to what has been internalized and so always moving on as a dynamic focus of forces ever changing. In this way the concept of "the unconscious" becomes the more understandable—one of unconscious processes whereby the organism adjusts to life demands, and whether these processes are labeled physiologic or psychologic is of rather academic importance.

It has become increasingly essential for me to base work with children and explanations to parents, teachers and social workers on these and similar concepts. Advice and theorizing without some grasp of the underlying physiology becomes armchair mental gymnastics and often turns into obvious platitudes. I have found a considerable number of such patients and clients willing and able to accept some explanation of behavior along these lines. Once one has begun to have concepts of how marvelously the organism as a whole functions in the adaptation to problems of everyday life, behavior assumes more of meaning. And yet this meaning is not of a dramatic or lurid character. It remains rooted in the chemistry, mechanics and purposeful psychology of the individual—it is significant, and our efforts as

physicians and as behavior workers are in the direction of learning more of any or all of these phases as we may.

## SUMMARY

Work in the field of mental hygiene has stressed the unit functioning of the organism. It has given support to the views that the vegetative nervous system and ductless glands are intimately involved with personality and behavior. It has furthered ideas of the essential similarity of experience in the individual's life—experience that may be affectional, infectious, traumatic, learning, or the like. Personality reactions may be as truly organically grounded as fever; fever may be as important psychologically as personality reactions. Treatment situations of whatever sort inevitably involve more than the specific technical procedure. Much of what happens is not clearly conscious to either physician or patient but becomes more understandable when viewed in part as physiologically characterized functions.

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## ABSTRACT OF DISCUSSION

DR. L. D. BRISTOL, New York: It might be well to take a moment to touch on the subject of mental health in industry. The business executive, while he unconsciously is thinking in terms of mental hygiene, is talking about "personnel relations" and "industrial relations"; a good many business executives don't like this term "mental hygiene" for some reason or other. One company of which I have knowledge for several years has carried on a program of so-called employee interviews, under trained interviewers, which are intended to iron out many of the worries and the maladjustments among employees. I am convinced that, with the shorter work day and the shorter work week, mental health in industry or mental health generally becomes more and more of a problem. The more a worker has time to worry about his job, to get a perspective on what he doesn't like in his job, the more difficulty there is going to be, and I should like to suggest the importance of developing more adequate leisure time activities among the industrial population. In this connection, a real program may be developed by some of the larger industries, but certainly for the smaller groups of employees, community agencies for more recreational and constructive leisure time activities would seem to be in order.

DR. HENRY A. LUCE, Detroit: When it comes down to practical things, it really doesn't matter in our first broad approach to the subject whether we are exactly technically correct—not that I don't want to have a diagnosis and know the value of diagnosis, but there are many general principles contributing toward mental health that can be utilized. For instance, there is the remark that we should provide for the recreational time, for the time in which the man is not employed, and the hours of employment are becoming rapidly less all the time. Some one said once that it is not what we do when we work that hurts us; it is what we do when we don't work. I hope that the spirit of approaching this matter from the point of preventive medicine, to relieve the high incidence of mental ill health, will prevail. I like that term "mental health" very much better than "mental hygiene." I hope that the effort we have started today will go on.

**Invention of the Compound Microscope.**—It is not known with certainty who invented the compound microscope and an extensive literature exists on the subject. The rival claims of Italians and Dutchmen have been carefully dealt with by Harting, who finally came to the conclusion that the credit lay between Cornelius Drebbel of Alkmaar (N. Holland) and the two Janssens, Hans and Zaccharias, of Middelburg. In the opinion of Harting the invention took place in Middelburg (near Flushing) before 1610 and possibly about 1590.—Bulloch, William: *The History of Bacteriology*, London, Oxford University Press, 1938.

## EIGHTY-SIX CASES OF CHRONIC SYNOVITIS OF KNEE JOINT TREATED BY SYNOVECTOMY

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The excision of a chronically inflamed synovial membrane for the relief of pain and the improvement of function in a joint is a relatively recent surgical procedure, its general use in this country being confined to the past fifteen years. The first synovectomy is said to have been performed by Volkmann<sup>1</sup> in 1877 in a case of tuberculous synovitis of the knee, but the operation seems to have fallen into disrepute after the prompt recurrence of the disease in this first case. In 1899 the Frenchman Mignon<sup>2</sup> published the first paper concerning synovectomy, and, although Goldthwaite<sup>3</sup> in 1900 and John B. Murphy<sup>4</sup> in 1916 reported cases in which they had performed the operation, it was Swett<sup>5</sup> of Hartford who in 1923 drew the attention of the orthopedic profession in this country to the possibilities of synovectomy and to some of the factors in the proper selection of cases. To Swett's original case report and to that of Ellis Jones<sup>6</sup> of Los Angeles made in the same year, the surgeon is indebted for the following rules governing the selection of cases for the successful performance of synovectomy:—

1. The operation should be performed only in cases of non-specific arthritis.
2. The disease should be localized in the synovial membrane with little or no involvement of cartilage or bone.
3. The patient should have had all foci of infection removed if feasible.
4. Conservative treatment should have been given adequate trial.
5. There should be considerable effusion within the joint.
6. The disease should be confined to one or, at most, to two joints.
7. The acute inflammation should have subsided.

It should be of value to analyze the results of a relatively large number of synovectomies, especially since in some of the cases there was wide deviation from the rules suggested by Swett and Jones while in others the selection conformed closely.

The following analysis is based on the late results of eighty-six complete synovectomies of the knee joint performed at the New York Orthopaedic Hospital between 1923 and June 1937. Partial synovectomies, synovectomies of other joints (one ankle, one elbow) and operations for which follow-up data are inadequate are excluded. The average follow-up period was 5.6 years, none being shorter than six months.

Nine of the knees operated on were the site of specific lesions in the synovial membrane. The nature of these lesions is indicated in table 1.

Synovectomy was performed in the cases of tuberculosis only because of mistaken diagnosis, and rapid

From the New York Orthopaedic Dispensary and Hospital.

Read before the Section on Orthopedic Surgery at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

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3. Goldthwaite, J. E.: Knee Joint Surgery for Nontuberculous Conditions, *Boston M. & S. J.* **142**: 286, 1900.
4. Murphy, J. B.: Synovial Capsulectomy in Hypertrophic Villous Synovitis of the Knee, *Surg. Clin. S.* **155**, 1916.
5. Swett, Paul P.: Synovectomy in Chronic Infectious Arthritis, *J. Bone & Joint Surg.* **5**: 110 (Jan.) 1923.
6. Jones, Ellis: Synovectomy of the Knee in Chronic Arthritis, *J. A. M. A.* **81**: 1579 (Nov. 10) 1923.

recurrence of the disease, requiring fusion of the knee, was the fate in all six cases. In the other three cases of specific lesions there also was recurrence after the synovectomy. In the cases of tuberculosis the longest interval between synovectomy and fusion was four months. Although it is realized that this does not provide an adequate test of the usefulness of synovectomy in the treatment of tuberculosis, the intense and rapidly progressing inflammation found at the second operation make its further trial in the case of tuberculous synovitis unwarranted. It is difficult to imagine

TABLE 1.—Cause of the Specific Lesions

	No. of Cases
Synovial tuberculosis.....	6
Hemangioma of synovial membrane.....	1
Echinococic disease.....	1
Osteitis of the tibia.....	1

making an earlier diagnosis of tuberculous synovitis than was made in these six cases; they were perfectly selected for a successful result if synovectomy is ever to be successful in the treatment of this disease, and yet the operation failed in all of them.

It is to the remaining seventy-seven cases, of chronic nonspecific arthritis of the knee, that especial attention is to be devoted in this paper. The operations were performed on fifty-eight patients, there being nineteen bilateral synovectomies. The oldest patient was 70 and the youngest 6, and the average age for the series was 36.1 years.

The cause of the synovial inflammation in these cases differed widely (table 2). Not only has synovectomy been performed on knees with subsided chronic non-articular synovitis in cases which fulfilled the conditions mentioned by Swett and Jones, but the procedure has been tried in several cases of rheumatoid arthritis in an effort to alter the course of the disease. Also, synovectomy has been performed on several painful osteoarthritic knees which were the site of secondary synovial hypertrophy. In nine cases the synovitis was traceable to chronic trauma, such as torn menisci or loose bodies, and six joints were affected by synovial osteochondromatosis.

A few of the patients had had excellent and consistent preoperative conservative treatment, to which they had not adequately responded; but the preoperative treatment of the majority had been inconsistent and sporadic, as is inevitable with the usual clinical type of arthritic patient, who wanders from one hospital to another in search of treatment. The whole series had sought relief from conservative therapy for an average of 5.2 years before coming to synovectomy.

Preoperative clinical laboratory work as a whole did not yield remarkable information, having proved to be of little use in the selection of cases except for the serologic tests to exclude syphilis and the determinations of the erythrocyte sedimentation rate to determine the activity of the synovial inflammation. No patient with a positive Wassermann reaction has been subjected to synovectomy in this hospital, since in all the cases of supposed syphilitic synovitis the condition has cleared up with antisyphilitic treatment. The first determination of the erythrocyte sedimentation rate in this series was done in 1933, and since 1935 this test has been part of the routine preoperative work-up. It gives a new criterion of the activity of arthritis, being more

accurate in this respect than ordinary physical and roentgenographic examinations. In the present series twenty-one patients had determinations of the sedimentation rate, and, although this number is small for the drawing of conclusions, it is suggestive that in the patients with normal rates 85 per cent of the operations gave satisfactory results whereas in the patients with elevated rates only 60 per cent resulted satisfactorily. In the majority of the cases synovectomy had no permanent effect on the sedimentation rate. It is much safer to defer synovectomy until bed rest and conservative antiarthritic treatment have reduced the sedimentation rate if to do so is feasible.

Roentgenographic studies of the joints are of use in arriving at a diagnosis and in ruling out specific lesions; unfortunately they have been of little help in attempts to prognosticate the outcome of synovectomy in any given case.

The operative technic was fairly uniform in most of the cases, although the operations were performed by twenty-eight different surgeons. Two vertical parapatellar incisions were usually made. This approach gives adequate exposure of the joint and does not interfere with the extensor tendons; thus splinting becomes unnecessary and motion may be instituted from the time of operation. The synovial membrane was excised from the anterior compartment and suprapatellar pouch only, except in one case, in which there was a herniation into the popliteal space and a separate operation was required. The infrapatellar fat pad was removed as a routine. In six cases the menisci were normal in appearance and were left undisturbed, and in two others one normal meniscus was left in situ. The good results obtained in these eight cases would seem to contradict the opinion sometimes expressed that menisci should always be removed in synovectomy because of supposed interference with their nutrition or attachments by the operation. All the operations were performed with a tourniquet, which in each case was not removed until the wound had been closed and a flannel pressure bandage applied. I believe that the

TABLE 2.—Cause of the Nonspecific Lesions

	No. of Cases
Rheumatoid arthritis .....	26
Osteo-arthritis .....	20
Chronic proliferative synovitis (includes 9 cases of trauma and 6 of osteochondromatosis).....	31
Total.....	77

technic and results would be improved if the tourniquet was removed and hemostasis effected before closure of the wound.

Postoperative care was consistent in that gentle passive and then active motion was begun within forty-eight hours after operation in almost all cases. Traction was applied for from one to two weeks in twelve cases, with no noticeable improvement in the outcome as compared to cases in which it was not used. In none of the knees did instability develop because of the operation, but two knees (both in cases of rheumatoid arthritis) required wedging plaster splints subsequently for the correction of flexion deformities. None of the joints were manipulated under anesthesia after operation.

The only postoperative complication was a slight transient tourniquet paralysis which cleared up com-

pletely. There were no deaths and no wound infections. Postoperative physical therapy, in the form of exercises and massage, was prescribed as a routine but varied greatly in the thoroughness with which it was carried out. The patients with the poorest results from synovectomy usually persisted longest in the physical therapy treatments.

Bacteriologically the knee joints yielded nothing of particular interest. There is a record of cultures of material taken from the joint at operation in all but the earliest cases, and in only one was there grown an organism of possible etiologic significance—a short-chained hemolytic streptococcus from one knee in a case of bilateral involvement. The only other positive cultures were of contaminating organisms such as *Staphylococcus albus* and *Bacillus subtilis*. It should be noted, however, that no special culture mediums were used and no consistent anaerobic work was done in an effort to isolate bacteria from the joints.

The pathologic changes in the synovial membrane, on the other hand, make an extremely interesting study. Typical monarticular chronic villous synovitis, which constituted the disease in most of the cases, probably cannot be classified under either of the great, commonly accepted divisions of rheumatoid arthritis or osteoarthritis. Pemberton<sup>7</sup> recognized this difficulty and stated that such synovitis should probably have separate classifications, such as chronic infectious and chronic traumatic arthritis. We have seen it in a few cases prove to be the precursor of generalized rheumatoid arthritis, there being two such cases in the series under discussion.

The clinical appearance of the joints and the gross pathologic changes seen at operation are familiar to all orthopedic surgeons, so they will not be dwelled on. Sections of the synovial membrane are remarkable because of one generalization that may be made from them: Whatever the cause of the inflammation, whether rheumatoid arthritis, infectious synovitis or chronic trauma, and regardless of what the clinical result of the operation may be, the pathologic changes in the synovial membrane are basically the same in all cases. They consist fundamentally of, first, hypertrophy and hyperplasia of the synovial layer of cells, so that this membrane is thrown into large villi and redundant folds, and, second, of thickening of the subsynovial layers by edema, fibrosis, engorgement of blood vessels, and scattered foci of round cell infiltration. Any one of these features may predominate in any given knee joint, but all are usually present in every case and with remarkable similarity, even in cases of osteoarthritis and of synovial osteochondromatosis. The round cell infiltration is usually perivascular and characterized by the presence of large numbers of plasma cells, thus simulating the histologic appearance of certain syphilitic lesions. In any attempt to correlate the histologic picture with the end result of the operation or to base a prognosis on the appearance of the microscopic sections, there has been a complete lack of success. Two sections which appear identical under the microscope may come from patients whose clinical courses differ completely.

Just why synovectomy should relieve pain in an arthritic joint has been the subject of some speculation. It is known from the work of Key<sup>8</sup> and others that

in the joints of experimental animals synovial membrane regenerates very promptly after its complete excision. Swett<sup>9</sup> has opened human knee joints at varying intervals after synovectomy and has found a regenerated membrane almost indistinguishable pathologically from that excised at the first operation. We have had a similar experience in two cases and have seen the reappearance of inflamed, hypertrophied synovial membranes after synovectomy in knees which were actively inflamed at the time of operation. I have not been able to find any published works on, nor have I had the opportunity of studying, the regeneration of the complicated nerve endings in synovial membrane after synovectomy, such as Gerneck<sup>9</sup> of Würzburg has observed in normal synovial membranes. These neural end organs undoubtedly regenerate after synovectomy, so that relief from pain is probably not due to their permanent extirpation; otherwise sensation and synovial secretion would be subnormal after this operation, which is not usually the case. As the synovial mem-

TABLE 3.—Results According to Diagnosis

	Rheuma- toid Arthritis	Osteo- arthri- tis	Chronic Syno- vitis	Total	Properly Selected Cases
Number of patients.....	19	13	26	58	19
Bilateral involvement.....	7	7	5	19	3
Number of synovectomies....	26	20	31	77	22
Age of oldest patient, yrs....	59	70	59	70	50
Age of youngest patient, yrs..	7	34	6	6	10
Average age, yrs.....	37.1	54.4	26.3	36.1	22.5
Average duration of symp- toms, yrs.....	5.9	7.8	3.4	5.2	3.2
Number of patients improved anatomically.....	12	14	26	52	19
Percentage improved ana- tomically.....	46	70	84	67.5	86.4
Number improved symptom- atically.....	16	18	27	61	21
Percentage improved symp- tomatically.....	61.5	90	87	80	95.4
Number improved function- ally.....	9	12	19	40	16
Percentage improved func- tionally.....	34.6	60	61	52	72.7
Number of joints now practi- cally normal.....	1	0	13	14	13
Percentage of normal joints..	4	0	42	18.2	60

brane is certain to regenerate, the success of synovectomy in the relief of pain would seem to depend on the regeneration of a relatively normal, thin, glistening membrane rather than on the regeneration of one also inflamed and hypertrophied. This constitutes a plea for the performance of the operation only when all active inflammation in the joint has subsided. In osteoarthritic knees the synovial hypertrophy is probably a reaction to the constant trauma caused by degenerated menisci, impinging osteophytes or loose bodies, and removal of these is the chief factor in the relief obtained.

#### RESULTS OF OPERATIONS

It will be remembered that 100 per cent of the synovectomies for specific lesions discussed earlier in this paper resulted in failure.

Of the seventy-seven knee joints with nonspecific, chronic proliferative synovitis in which synovectomy was performed, satisfactory results from the operation can be said to have been obtained in fifty-seven, or 74 per cent. A "satisfactory" or "improved" result in this study is one in which there was complete or considerable relief from pain, with some improvement in function or

7. Pemberton, Ralph: Arthritis and Rheumatoid Conditions, Philadelphia, Lea & Febiger, 1929.  
8. Key, J. A.: Reformation of Synovial Membrane in Knees of Rabbits After Synovectomy, J. Bone & Joint Surg. 7: 793 (Oct.) 1925.

9. Gerneck, I.: Ueber die Nerven der Synovialmembran, Arch. f. orthop. 28: 599 (July 23) 1930; Ueber die Innervation der Synovialmembran beim Menschen, Ztschr. f. Anat. u. Entwicklungsgesch. 97: 515, 1932.

at most very little loss of function. For example, when all pain was relieved but most of the motion was obliterated by the operation the result was considered a failure, as it was when the synovitis recurred or when, as in several of the cases, the improvement did not follow the synovectomy but ensued after the removal of foci of infection several months later. The statement, therefore, that 74 per cent of the patients were improved by synovectomy means little unless the cases are analyzed according to the diagnosis and according to the anatomic, symptomatic and functional aspects of the results.

Synovectomy was performed on twenty-six knees which were affected by definite rheumatoid arthritis. In some of the cases the operation was done deliberately in an effort to alter the course of the disease, and in others the true nature of the arthritis did not become apparent until some time after the operation. Next to the patients with specific lesions, the group with rheumatoid arthritis responded most poorly to synovectomy. Only 61 per cent of the patients with the latter condition were improved symptomatically by the operation, and only 34 per cent were improved functionally. The rest either had recurrence of their lesions or were actually made worse by the operation.

Twenty painful and disorganized osteo-arthritic knees were operated on. As there is always considerable involvement of cartilage and bone in such knees, synovectomy is theoretically contraindicated. However, symptomatic relief was obtained in 90 per cent of the cases, and 60 per cent of the knees were improved functionally. Indeed, some of the most satisfactory and even dramatic results were seen in elderly patients with osteo-arthritis, several of whom were released from bed or wheel chair and restored to relatively active lives by the operation.

In the group affected by simple chronic proliferative synovitis there were thirty-one patients, including those with synovitis due to chronic trauma and those showing osteochondromatosis of the synovial membrane. The results in this group were about the same as in the osteo-arthritic group: 87 per cent improved symptomatically and 61 per cent functionally. However, among these patients nine who were operated on had obvious foci of infection; if these ill selected patients are excluded, there are twenty-two properly selected cases which fulfilled practically all the conditions suggested by Swett and Jones, and the percentages rise significantly. The figure for satisfactory symptomatic results becomes 95.4 per cent and that for functional improvement 72.7 per cent. These are very gratifying figures for any surgical procedure. Furthermore, in thirteen of these twenty-two properly selected cases, or 60 per cent, practically normal joints were obtained; the results were excellent anatomically, symptomatically and functionally.

All the knees with chronic traumatic synovitis or with synovial osteochondromatosis showed symptomatic and functional improvement after synovectomy.

It will be noted from table 3 that synovectomy offers the most promise for symptomatic improvement and that the figures for anatomic improvement (correction of flexion deformities, swelling) come next and those for functional improvement last.

The importance of effusion within the joint has often been stressed in the proper selection of cases for synovectomy. In this series of cases, fifty knee joints con-

tained excess synovial fluid at operation and twelve were described as dry, while in the remaining fifteen cases the fluid was either normal in amount or the surgeon's note was inadequate for the determination of this point. Synovectomy resulted in failure in 50 per cent of the cases in which the joint was dry, while satisfactory results were obtained in 75 per cent in which the joint was wet. As most knees with rheumatoid arthritis contain excess fluid, it should be remembered that extensive effusions are of good omen only in cases of nonrheumatoid arthritis.

Attention should be called to the fact that when recurrences of the synovitis take place after synovectomy they occur within a few weeks or not at all and that in observing the improved joints over a number of years it is found that improvement continues progressively, so that the five year result in a given case is as a rule better than the result one or two years after operation.

#### CONCLUSIONS

1. In a properly selected case of chronic, nonspecific, proliferative synovitis of the knee, synovectomy offers a 95 per cent chance of improvement and a 60 per cent chance of restoring a practically normal joint.

2. Patients with an osteo-arthritic knee which is the seat of secondary synovial hypertrophy with effusion often have gratifying results from this operation, 90 per cent of those in the present study having obtained symptomatic improvement.

3. For rheumatoid arthritis synovectomy cannot be depended on to give symptomatic relief in more than about half the cases, and many knees are made worse by the operation.

4. Tuberculosis of the synovial membrane is a strict contraindication for synovectomy, however early the diagnosis is made.

5. Failures of synovectomy are due more to improper selection of cases than to any other factor.

6. The rules for the proper selection of cases for synovectomy suggested by Swett and Ellis Jones in 1923 are still valid.

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#### ABSTRACT OF DISCUSSION

DR. DAVID H. KLING, Los Angeles: The result of Dr. Inge's comprehensive study showed the efficiency of synovectomy in carefully selected cases of synovitis. I agree with most of these requirements and I shall take up only a few additional points which Dr. Inge hoped would come out in the discussion. The rule of removing all the foci of infection is laudable, but I do not know how one can do it. There is no agreement as to which are important foci of infection in arthritis. Even the importance of the tonsils and the teeth was recently challenged by Robinson. Most important in deciding on operability is whether the joint is still the seat of infection. Dr. Inge uses the sedimentation test of the blood and I can confirm the usefulness of this simple test. I have tried to take another step in that direction. I have suspended a volume of the patient's blood corpuscles in the aspirated synovial effusion equal to that in the blood and have registered the sedimentation rate. I have found that rapid settling within the synovial effusion shows an active inflammatory process, while in chronic stages there is a very low sedimentation of the suspended blood corpuscles. A systematic examination of the synovial fluid is useful for prognosis. Characteristic for severe inflammations are synovial effusions which are turbid and have a low viscosity, a high cell count, a prevalence of granulocytes and a rapid sedimentation of suspended blood corpuscles. The prognosis in

these cases is doubtful, because inflammation and destruction are pronounced and the resistance of the synovial membrane is low. On the other hand, synovial effusions which are almost clear and have a high viscosity, a low total cell count, prevalence of lymphocytes, an increase in synovial cells and a low sedimentation rate indicate a predominance of hypertrophic changes in the synovial membrane. Such cases offer a good prognosis. I found that to be true in villous synovitis, in which Dr. Inge has had almost 95 per cent good results. The results which Dr. Inge has observed in osteo-arthritis indicate that this operation should not be delayed until the physical, moral and financial resources of the patient have been exhausted by futile treatments.

DR. J. ALBERT KEY, St. Louis: I agree about tuberculosis. Some of my happiest as well as worst results have been in rheumatoid arthritis. My principal quarrel with this paper is the classification. Osteo-arthritis presumably is not a disease of the synovial membrane. Likewise, what is chronic, non-specific villous arthritis? I do not know that any one has ever satisfactorily placed that condition. I believe that those are probably patients with a hypertrophic joint who have an added rheumatoid disease in that joint. I believe that all his patients with osteo-arthritis—there were twenty as I recall—also were of that type. In other words, if one is going to do a synovectomy one must have thickened synovial membrane to remove. In the straight osteo-arthritis the synovial membrane is not markedly changed and I believe that these patients had rheumatoid arthritis superimposed on an old hypertrophic arthritis. Recently Frank Dickson showed me some patients with typical severe, progressive, active rheumatoid arthritis on whom he had performed extensive synovectomies of the knee joints, always removing the semilunar cartilages and as much of the synovial membrane as he could get from the front. I think he used a long incision in which the patella was displaced laterally, and in a considerable percentage of these patients not only were the knees improved but the disease appeared to have been arrested. I think that is something we should investigate and I expect in selected patients in whom the disease is active with a painful, swollen, thickened knee joint to do synovectomies with the hope not only that I shall help that knee but that I shall arrest the disease.

DR. GEORGE A. L. INGE, New York: I agree with Dr. Kling that foci of infection cannot always be removed and that in many instances one cannot name the focus responsible for the arthritis. Yet the fact remains that in this series of cases the better results were obtained in those patients whose removable foci of infection were eliminated before synovectomy. In several of my cases in which the operation was performed in the presence of obvious foci of infection, such as chronically inflamed tonsils, the synovitis promptly recurred and persisted until tonsillectomy was performed subsequently. It would be desirable to save such patients the inconvenience of synovectomy. I have had no experience with the sedimentation rate of erythrocytes in synovial fluid. It is a very interesting observation. I admit that I may not know what chronic non-specific proliferative synovitis is, but I believe that Dr. Key will agree with me that the group of knees to which this term is applied presents a synovitis which is chronic, which is nonspecific, and which is characterized pathologically by proliferation of the synovial membrane; and he will also agree, I am sure, that often such knees may be observed for years without assuming the characteristics of rheumatoid arthritis or osteo-arthritis. Pemberton discusses in his book the difficulty of classifying these joints, and all of us are familiar with the difficulty of classifying individual cases of arthritis. The cases in the present series were classified as accurately as possible, but as always there were joints in which more than one type of arthritis was present. Certainly there is no need for synovectomy in a case of pure osteo-arthritis; but, as Swett has pointed out, many of these joints show secondary synovial hypertrophy, and it is these which give such satisfactory results after synovectomy. I also have seen a few dramatic results following synovectomy in rheumatoid arthritis, but unfortunately the statistics are against the probability of their frequent occurrence.

## PULMONARY EDEMA AND EMBOLISM

AS COMPLICATIONS OF INSULIN SHOCK IN  
THE TREATMENT OF SCHIZOPHRENIA

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In the published reports dealing with the insulin treatment of schizophrenia the tendency has been to stress indications, contraindications, methods and results. This procedure has tended to place before the physician a new instrument for his armamentarium without warning him of the dangers except to give statistically the mortality rate. Because the mortality rate is low and because the disease is so hopeless that almost any method offering help is welcome, the dangers have not been sufficiently explained. This report is offered in the belief that more benefit is at present to be derived from a citation of difficulties than from addition of material to the already large literature on methods and results.

Before presentation of cases a brief review of the circumstances leading to serious complications should be given. Good clinical results from the treatment depend on, though they are not directly proportional to, a certain severity or depth of reaction. It is not sufficient to allow merely severe stupor or mild coma to appear and to interrupt this by immediate administration of dextrose by mouth or vein. Such treatment is quite safe so far as the life of the patient is concerned but is relatively barren of results; it is necessary to reach in general a much deeper coma and to prolong this state so long as compatible with reasonable assurance of restoration of the patient to consciousness at the will of the physician. In general it can thus be said that the results vary directly as the danger.

There is no way known to us by which the effects of the insulin can be measured mechanically or chemically after the state of coma is reached. The dextrose concentration in the blood falls to a point too low to measure (if not to zero) long before the clinical state is reached by which the patient is to profit. There is nothing but experience and clinical judgment to guide one as to time of termination of the coma.

On the basis of clinical observations there is a point in the development and progress of cerebral pathologic process in insulin shock at which a radical change occurs such that administration of dextrose intravenously or otherwise does not alone suffice to revive the patient. He may still revive, but administration of dextrose does not alone bring this about; the other necessary element is time. This point, it seems to us, varies with different patients and with the same patient on different days. We have not discovered any accurate means to measure it. We are certain that we have allowed our patients to pass this point on many occasions; a wait of from thirty to forty minutes is not at all unusual. We have also had to wait sixteen, twenty and thirty-three hours respectively in three cases. During this time the clinical condition of the patient was good; there was no cyanosis, tachycardia or dyspnea; it was merely impossible to restore consciousness. Just after the periods mentioned the patient awoke as from a prolonged sleep and began to take cognizance of his surroundings; one or several hours later he spoke.



The application of these facts to the present problem is that when pulmonary edema supervenes the patient's brain cells may be in the immediately irreversible state and the prolongation of the coma may be unrelated to the complication. This most complex state of affairs was present in our first case of pulmonary edema and greatly added to our difficulty. Four cases are briefly presented to illustrate the problems and the manner of attempted solution:

#### REPORT OF CASES

**CASE 1.**—*Irreversible coma; pulmonary edema, then apnea after seventh treatment; recovery from sixteen hour coma after treatment with dextrose, atropine, coramine, epinephrine, caffeine and artificial respiration by pulmotor; continuation of insulin therapy, with good therapeutic result.*

H. C., a girl aged 19 years, was referred by Dr. K. G. Burchard of Hollywood in excellent physical condition before treatment was begun. Indications for treatment were paranoid delusions and active violent negativism, in spite of good retention of intellect. Treatment was begun Sept. 15, 1937, with intramuscular injection of 50 units of insulin, which produced only a period of drowsiness followed by one of active quasivoluntary psychomotor excitement. This was terminated after four hours by administration of sweetened orange juice.

The second treatment was given on the following day with 80 units; it produced even less reaction, only drowsiness. On the third day 140 units was given, resulting only in drowsiness and nystagmus. A day of rest then was passed as a routine, and the fourth treatment was given September 19, with 190 units and, as usual, without breakfast. This produced drowsiness after one hour, followed by slight tremors. After two and one-half hours coma and a Babinski sign (on the left) appeared and at three hours dissociated movements of the eyeballs appeared. Then came bulbar symptoms and at four hours decerebrate rigidity and vertical nystagmus. Administration of dextrose by nasal tube brought prompt restoration of consciousness.

September 20 and 21 the dose was 210 units of insulin and the days were not remarkable, being practically identical with September 19. Restoration of consciousness was prompt on each day after decerebrate rigidity had appeared.

September 22 was an eventful day, and the details form the subject at hand. The dose was again 210 units (as on the two previous days). After one and one-half hours the patient went into a quiet sleep. The pulse rate was 68 and the respiratory rate 18 per minute. Two hours after the injection of insulin the pulse rate fell to 60 per minute and the respirations began to increase in number. At two and one-half hours decerebrate rigidity appeared, but it disappeared spontaneously at three hours and a bilateral Babinski sign appeared.

Dextrose was now given by nasal tube, but instead of regaining consciousness the patient remained in coma, and fifteen minutes later violent writhing and twisting (torsion spasm) developed. Saline mixture and more dextrose solution were given by tube but it became evident that intravenous administration of dextrose was indicated. Because of the severe torsion spasm the needle was jerked out of the vein so often that it was necessary to enter eight times in order to give 25 cc. of 50 per cent solution. Severe athetosis then appeared and the respirations became rapid.

Four and one-half hours after injection of the insulin droplets of a thin mucoid secretion began to be expelled with the respirations, and a diagnosis of pulmonary edema was made. The patient was turned face downward and everything was done to facilitate drainage of the fluid, which was profuse, from the mouth and nose. Intramuscular injections of caffeine with sodium benzoate were given, followed by injections of epinephrine hydrochloride (1:1,000), of coramine (25 per cent pyridine betacarboxylic acid diethylamide; three ampules in an hour) and of digifoline (two ampules). As the patient became more quiet a surgeon was called to expose a deep vein and give 100 cc. of 50 per cent dextrose solution (the veins having collapsed).

The edema increased, the patient became cyanotic and a pulmotor apparatus was obtained from the fire department. Before it appeared the patient ceased breathing and a deep purple color developed. Artificial respiration was instituted, and when an

oxygen-carbon dioxide mixture (carbogen) was given by inhalation spontaneous respiration was restored. The pulmonary edema lasted four hours, after which rales could no longer be heard and the patient's clinical condition was good but the temperature was 101 F. She was placed in an oxygen tent until 3 o'clock the next morning, when she regained consciousness (after sixteen hours of coma). The temperature promptly became normal.

The patient was not treated during the following four days; then injections were begun of 50 units of insulin. The dose was increased until, after seven days, 150 units daily was given. This became the regular dose, and the treatment was finished November 14. The patient showed little mental improvement for a month but then became apparently normal; she returned to her school work, in which she has continued to date (March 1938).

After this experience a resuscitation outfit was always kept on hand, and we feel that we were not so well prepared for emergencies as we should have been before undertaking the treatment at all. Good fortune had been responsible for the successful management in sixteen prior cases.

**CASE 2.**—*Pulmonary edema after thirty-first treatment; immediate restoration to consciousness by intravenous injection of dextrose; progress of edema; recovery after treatment with atropine, coramine, epinephrine, caffeine, oxygen-carbon dioxide taken by inhalation, and morphine sulfate; continuation of treatment, with results not yet known.*

D. P., a white man aged 29, was treated because of paranoid delusions, confusion and negativistic behavior; he had good retention of intellect. Treatment was begun Jan. 9, 1937, with an initial dose of 50 units given intramuscularly (no breakfast). The dose was gradually increased to 130 units daily. The patient was somewhat unusual in that he produced daily large quantities of mucus in the throat, which required continual aspiration (with a centrifugal aspirator) during each treatment. He did not show pulmonary edema until the thirty-first treatment was given.

On February 16, when he was in coma, a nasal tube was passed for the purpose of administering dextrose. He immediately ceased breathing, and the tube was withdrawn without the solution having been given. An intravenous injection of dextrose (20 cc. of 50 per cent solution) was administered; this immediately revived him, but he was dyspneic. The dyspnea increased and the patient began to cough up quantities of pink mucus. Examination showed extensive pulmonary edema of the left side only and treatment for that condition was instituted. The patient became very cyanotic and the dyspnea agonizing.

While an oxygen-carbon dioxide mixture was being given, atropine, epinephrine, coramine and digitalis were given hypodermically. The pulse rate increased to 150 beats per minute. As the patient was of necessity in a prone position, it was difficult to give dextrose solution intravenously, but a vein coursing along the achilles tendon was entered and 100 cc. of 50 per cent solution of dextrose administered. After two hours of improvement the patient relapsed, and it was found that the edema had spread to the right side. A medical consultant then recommended  $\frac{1}{4}$  grain (0.015 Gm.) of morphine sulfate, which gave rapid relief. After six hours the patient was comfortable. Treatment was resumed after three days and at the time of writing is still in progress. No further untoward reactions have appeared, although dyspnea occurs daily.

It was fortunate that the patient could be restored to consciousness so easily, and his cooperation throughout was invaluable. Previous experience with the condition expedited early diagnosis and treatment.

**CASE 3.**—*Severe dyspnea on seventh day of treatment; dextrose given by nasal tubing and intravenous injections; sudden appearance of severe pulmonary edema; extreme cyanosis, dyspnea and tachycardia; recovery after intravenous injection of dextrose, intramuscular injection of coramine and treatment with digitalis, epinephrine, caffeine with sodium benzoate, morphine with atropine and oxygen taken by inhalation.*

C. H., a white man aged 21, was referred by Drs. Harding and Cummins of Santa Monica for treatment because of confusion and violent negativism, with a paranoid trend. There was

nothing unusual about the treatments until the fifth was reached, March 4, 1938, when the patient received 120 units of insulin and after three hours became markedly dyspneic while in coma. The alae nasi collapsed and the lips were sucked inward with each breath. Although it was too early from the standpoint of duration of the coma, the patient was given by nasal tube a solution of dilute syrup. While this was being administered he went into deeper coma, for which reason 20 cc. of dextrose solution (50 per cent) was given intravenously. He immediately responded and remained clear for the day.

March 5 was rest day. On the sixth the same dose (120 units) was given, with the thought that an intravenous injection would be administered instead of the intranasal tubing of syrup. However, the patient merely went into a quiet sleep after two hours, awakened at two and one-half hours and did not go into a coma. Dextrose solution was administered by nasal tube to neutralize the excess insulin. After such different results with the same dose, an equal injection was administered March 7, with a resultant course entirely different.

March 7 the coma was allowed to continue until the fourth hour because the patient remained in good condition. During the nasal feeding with dextrose he was dyspneic, as on March 4, and again 20 cc. of 50 per cent dextrose solution was administered. The patient regained consciousness promptly but began to exhale and expectorate large quantities of frothy mucus tinged with blood. One-eighth grain (0.007 Gm.) of morphine sulfate and  $\frac{1}{500}$  grain (0.0004 Gm.) of scopolamine hydrobromide were given hypodermically. The dyspnea was not marked and the patient was considered in fairly good condition, as he was only slightly cyanotic.

With dramatic suddenness the patient became extremely cyanotic, the entire body became characterized by purple lividity and the dyspnea became agonizing. Coramine and atropine with digitalis were given intramuscularly, and oxygen inhalation was begun. Then 50 cc. more of dextrose solution (50 per cent) was given, and the patient gradually improved. The expectorated fluid was blood tinged but it finally ceased appearing.

At the ninth hour there was a sudden relapse, with more dyspnea and cyanosis. Rales again appeared over the left lung. The pulse rate increased to 168 beats per minute and the respiratory rate to 30. Coramine was given intravenously, digitalis intramuscularly and another 50 cc. of dextrose solution of the usual strength intravenously. One-fourth grain of morphine sulfate and  $\frac{1}{100}$  grain (0.0006 Gm.) of scopolamine hydrobromide were then given. The rales rapidly subsided, and improvement continued. The administration of oxygen was continued until the fourteenth hour, and the dyspnea gradually disappeared. Retention of urine was present for another six hours.

This case illustrates the great variability in a given patient's reaction on various days and also how difficult it is to judge the best method of restoring consciousness.

The three cases represent our experience with pulmonary edema associated with insulin shock treatment, and in communications to us other men have reported similar difficulties, not always with a favorable outcome. We look on this complication as the most distressing one can encounter.

*CASE 4.—Sudden nausea, vomiting, profuse perspiration and collapse two hours after completion of an insulin treatment and after the noon meal had been normally consumed; severe cyanosis, pain in chest and dyspnea, with gradual recovery after use of stimulants; next day partial ileus and tarry stools, but with subsidence; continuation of treatments and good clinical results.*

M. B., a youth aged 19, had had eight usual treatments, with the usual course. After the ninth treatment he was given the usual dinner and, feeling well, he ate with relish. At 2:30 p. m., when he was considered settled for the day and the physician in charge had left the sanatorium, the patient became nauseated and went to the bathroom to vomit. The nurse in charge followed him to determine the reason for his apparent uncertain gait. In the bathroom he sank to the floor, became almost pulseless and broke into a profuse perspiration. He became severely cyanotic in a few minutes, and his respirations were short and grunting. He complained between breaths of severe pain in

the chest. The physician was called, and the patient put to bed, and stimulants were given. The cyanosis increased to a deep purple lividity.

When the physician arrived half an hour later the patient had greatly improved through the use of caffeine with sodium benzoate, epinephrine, coramine and oxygen, but he was still suffering with considerable dyspnea and was coughing up mucus. Some cyanosis was still visible, but this became less without further treatment during the next hour. The dyspnea ceased after eight hours.

We were not certain what sort of complication had occurred, but the question was answered almost certainly by the appearance the next morning of abdominal distress, partial ileus, distention and the appearance of black sticky stools. With medical management and only local treatment these manifestations all disappeared in three days. The course of treatments was then completed without further complications and with good clinical results.

We consider this a case of pulmonary embolism, though the source of the embolus has not been discovered. Previous intravenous injections of dextrose solution (50 per cent) had been administered, and it is possible, in spite of the lack of local evidence, that an embolus arose in the veins of the arm. At any rate, the sudden collapse, dyspnea, pain in the chest, profuse perspiration and subsequent evidence of secondary embolism to the bowel seem to make the diagnosis certain.

#### COMMENT

Mild states of pulmonary edema are doubtless common with insulin shock. The diagnosis is made difficult by the restless uncooperative state of the patient and by the accumulation of mucus in the nose and throat, which precludes auscultatory information relative to the lungs. Clinical guides to indicate severe edema seem to be rapid shallow breathing or grunting dyspneic respiration in the presence of mucus in the throat. However, these signs often occur without supervention of pulmonary edema and are therefore merely warning signals. Pulmonary embolism is probably very rare in patients being treated with insulin shock but evidently needs to be considered.

These four serious instances occurred in twenty-six cases (in only twenty of which was treatment completed), or about 1,200 treatments. This percentage may appear low, but when one considers that in about one case in seven a threatened fatal outcome is apparently apt to develop and that if we had not been extremely fortunate we might easily have had four fatalities to report, there is good reason for any one attempting the treatment to give careful consideration to its dangers.

We have nothing new to offer for the treatment of pulmonary edema. One first attempts to restore the patient to consciousness. Atropine (so generally recommended) aids in preventing the production of mucus in the lungs but it certainly does not suddenly prevent or cure the edema. Morphine seems indicated unless possibly in the case of approaching apnea, when further suppression of respiration may be a contraindication. Epinephrine probably helps to dilate the bronchioles, and caffeine stimulates respiration. Oxygen is of great benefit when the respiratory area in the lungs has been much reduced by the swelling of the alveolar walls.

#### SUMMARY AND CONCLUSIONS

Pulmonary edema developed in three cases and pulmonary embolism in one during insulin shock treatment for schizophrenia. These are serious dangers, one of which is apt to occur in about one case in seven, as in our series of twenty-six cases (in only twenty of which

was treatment completed). There is little comfort in the statistical statement that these three instances came in 1,200 treatments, since each patient receives normally at least fifty shocks. Before a patient is given insulin treatment one must be prepared not only to restore consciousness lost through insulin shock but to treat acute and possibly fatal pulmonary edema with every means known for resuscitation.

In treating pulmonary edema one first attempts to restore consciousness by intravenous injection of dextrose; the patient then takes oxygen or oxygen-carbon dioxide mixture by inhalation, the physician simultaneously administering atropine, epinephrine, coramine, caffeine and morphine intramuscularly. With these measures and good fortune it is possible to save patients who otherwise would rapidly die.

727 West Seventh Street.

## SALMONELLA PANAMA

OCCURRENCE IN SERIOUS INFECTIONS OF INFANTS  
IN NEW YORK CITY

FRITZ SCHIFF, M.D.

NEW YORK

It is of special interest to record the occurrence in New York of a bacterium belonging to the paratyphoid or *Salmonella* group, which has been reported only once before, in 1934, from cultures sent by E. O. Jordan in Chicago to F. Kauffmann in Copenhagen. The organism in question had been recovered during the study of an outbreak of food poisoning among American soldiers in Panama. The culture, according to Kauffmann,<sup>1</sup> had distinct serologic characters and was listed as a new type, *Salmonella panama*.

The paratyphoid or *Salmonella* group, named after D. E. Salmon, once a co-worker of Theobald Smith, includes several types or species causing enteric fever or gastro-enteritis. For many years three main types of *Salmonella* have been considered as a cause of food poisoning:

1. Bacterium or *Salmonella aertrycke* (other names: *Bacillus breslaviensis*, *Bacterium pestis caviarum*, *Bacterium typhi murium*, mutton type),
2. Bacterium or *Salmonella enteritidis*,
3. Bacterium or *Salmonella supefisteri*.

Frequently, however, cultures occur which in some respect differ from these three classic types. These "atypical" forms may be compared to the former group IV of pneumococci, which now has been separated into twenty-nine serologic types. In a similar way, numerous types or "species" of *Salmonella* have been established. A type list approved by the *Salmonella* subcommittee of the International Society for Microbiology is known as the Kauffmann-White table.<sup>2</sup> In the form which is reproduced in Topley and Wilson's<sup>3</sup> textbook on bacteriology it contains about fifty types. By means of this table it is possible to identify almost all the actually occurring *Salmonella* cultures. The Kauffmann-White table contains types reported from all over the world; the number of types to be considered

in any one country is, of course, much smaller. The use of the complete table, however, may be helpful for the identification of organisms that have previously been found only in other parts of the world.

For clinical use, the generic diagnosis "*Salmonella*" or the consideration of a few main types is sufficient, as no therapeutic procedure depends on its typing. The value of typing has to be sought in another field, namely in epidemiology. An outbreak of food poisoning due to *Salmonella* usually is caused by a single type. If more than one type occurs, it must be assumed that more than one source of food poisoning exists. It is evident, and confirmed by the study of many outbreaks, that the sources of single or group infections can be traced in a more exact and a more reliable manner when the type of *Salmonella* is considered. Several types of *Salmonella*, as their names indicate, for example, *Salmonella cholerae suis*, *abortus bovis* and *anatum*, are found more frequently in certain classes or species of animals than in others. Relations of this kind have sometimes been a definite help in the discovery of the animal origin of food poisoning.

### REPORT OF CASES<sup>4</sup>

**CASE 1.—History.**—S. D., a white baby boy, aged 11 months, was admitted to Beth Israel Hospital Nov. 22, 1936, with a history of an infection of the upper part of the respiratory tract and diarrhea of one week's duration. There were as many as ten stools a day with much mucus but no blood. The mother had diarrhea a few days before it developed in the child.

**Examination.**—Physical examination revealed that the child was well nourished and not markedly ill. The temperature was normal throughout the entire stay in the hospital (seventeen days). Clinical diagnosis was food poisoning. Laboratory examinations revealed the hemoglobin content 70 per cent, red blood cells 5,514,000, white blood cells 10,400. Stools contained no blood. Stool culture November 23 revealed *Salmonella* later identified as *panama*. Stool cultures November 28 and December 9 were negative. The urine was normal.

**Course.**—The infant's weight was normal on admission and increased steadily during his stay in the hospital. The infant had one or two loose green stools daily with no blood for the first few days. Thereafter, the stools had a normal appearance and consistency and remained normal until his discharge from the hospital December 7.

**CASE 2.—History.**—S. H., a white baby girl, aged 4 weeks, one of nonidentical twins, was born Aug. 5, 1937, in the Jewish Maternity Hospital in good condition and discharged August 20. August 31 she was admitted to Beth Israel Hospital with a history for the past four days of frequent soft and watery stools, vomiting and a loss of 10 ounces (284 Gm.).

**Examination.**—On admission the patient was moderately dehydrated but fairly well nourished, weighing 6 pounds, or 2,722 Gm. (birth weight, 6 pounds 1½ ounces [3,148 Gm.]). Except for fullness of the left ear drum, obscured landmarks of the right drum and a reddened throat, physical examination was essentially negative. Laboratory examination on admission showed hemoglobin 94 per cent, red blood cells 4,100,000, white blood cells 18,600, with 44 per cent polymorphonuclear leukocytes, of which 7 per cent were staff cells and 56 per cent lymphocytes. One stool culture was reported negative. The clinical diagnosis was bilateral otitis media, diarrhea and malnutrition.

**Course.**—In spite of various standard therapeutic measures for parenteral diarrhea, including several blood transfusions, the course was progressively downhill. The infant continued to lose weight and appeared marantic. The stools were continuously loose and yellow, averaging five a day. The benizidine reaction of stools was markedly positive. Stool culture Sep-

From the Bacteriological Department, Beth Israel Hospital.  
1. Kauffmann, F.: *Zentralbl. f. Bakt.* 132: 160 (Aug. 7) 1934.  
2. St. John-Brooks, R.: *The Genus Salmonella* Lignières, 1900: Issued by the *Salmonella* subcommittee of the Nomenclature Committee of the International Society for Microbiology. *Hyg.* 34: 333 (Oct.) 1934.  
3. Topley, W.: *The Principles of Bacteriology and Immunology*. Wood & Company, 1936.

4. Dr. Herman Schwarz gave the author permission to use the clinical records.

tember 1 was negative. The temperature ranged from 100 to 98.6 F., with one rise only to 102 on the third hospital day and a terminal rise to 101.8 F. shortly before death. After nine days' stay in the hospital paracentesis of both ears was performed and frank pus was obtained. Eighteen days after admission a terminal bronchopneumonia developed which was confirmed by roentgen examination. The infant died after twenty-five days in the hospital. Culture of the heart's blood taken immediately after death revealed organisms of the *Salmonella* group, later identified as panama.

**CASE 3.—History.**—J. B., a white baby boy, aged 5 months, was admitted to Beth Israel Hospital Oct. 14, 1937, with a history of from twelve to fourteen semiformed, nonbloody stools a day, fever of 103 F. and vomiting of two days' duration.

**Examination.**—On admission the child was well nourished, acutely ill and irritable. Skin turgor was fair. The ear drums were dull, red and slightly bulging; otherwise there were no abnormalities. Laboratory examinations revealed the blood count essentially normal. The urine showed 1+ albumin. The feces gave a slightly positive reaction for blood. Stool cultures October 15, negative; October 16 and 19, *Salmonella*; October 26, negative; November 1 and 2 *Salmonella*; November 5, negative. The organisms found were later identified as *Salmonella panama*. Clinical diagnosis was infectious enteritis, *Salmonella* group.

**Course.**—Diarrhea persisted for one week, after which the stools became less frequent. Cultures of the stool were positive for the *Salmonella* group for two weeks while the patient was in the hospital, after which time no blood or pathogenic organisms were found. The infant's temperature remained normal throughout the entire course of illness in the hospital. The infant gained in weight and was discharged in good general condition after a stay of twenty-three days in the hospital.

A fourth patient, who probably belongs to this group, was not listed because no positive bacteriologic abnormalities could be obtained. This infant was the twin brother of our patient 2.

**CASE 4.**—An infant, the twin brother of S. H. (case 2), became ill Aug. 20, 1937, with diarrhea and died September 2. A diagnosis of diarrhea and infection of the upper part of the respiratory tract was made. The postmortem examination showed emaciation and dehydration, bilateral bronchopneumonia, and hemorrhage beneath the epithelium in the urinary bladder. Considering the circumstances, it is likely that the infant suffered from the same infection as his sister.

#### COMMENT

All patients were infants from newly born up to 13 months of age. The clinical manifestations do not differ from other similar diarrheas. The seriousness of the infections is demonstrated by the deaths of the two youngest babies. It is well known that *Salmonella* infections are usually particularly dangerous for the very young. This experience applies to human beings as well as to natural and experimental infections of animals.<sup>5</sup> With our twins, the very hot weather may have influenced the course of the disease. The two other infections were not "summer diarrheas" in the exact sense, for they occurred in November and October. According to the history, however, the disease in case 1 may have begun during the hot season.

As to the source of the infections, definite statements were not made. In case 1, diarrhea in the mother previous to the condition in the baby is mentioned. The older literature reports several babies, among them newborn infants, infected by a mother who previously had been sick from food poisoning.<sup>6</sup> Occasionally the mother's milk has been found infected by the specific bacterium.

In our case, infection of the baby from the mother would be the natural assumption. Bacteriologic examinations of the mother, however, had not been done. The question of suspicious food could not be studied. At the time the bacteriologic diagnosis revealed the specific character of the disease it was too late to do so.

**Bacteriologic Examination.**—There were gram-negative motile bacteria, a rich growth on plain agar and on Endo medium and no formation of indole. Gelatin was not liquefied. There was no virulence for mice on feeding and no "wallbildung" of single colonies. They fermented dextrose, mannitol, maltose, xylose and dulcitol. There was a positive reaction in Stern's glycerol broth. They did not ferment lactose, saccharose or inositol. The reactions were in agreement with the generic diagnosis *Salmonella*.

**Serologic Examination.**—The cultures obtained from the three patients reacted definitely with some of our immune serums used for the routine diagnosis of *Salmonella*. The identity of these cultures was confirmed by Kauffmann, who after simple agglutination tests gave the diagnosis of *Salmonella panama*. However, they differed from his original culture in that they promptly fermented dulcitol.

For further study, a comprehensive examination was instituted in our laboratory. Immune serums for the three New York cultures and the original Panama strain were prepared. For comparison, about thirty cultures representing different types of *Salmonella* were available.<sup>7</sup>

The Panama type, as originally described, is characterized by a typical combination of four antigenic components. The immunization of rabbits with all three New York cultures yielded for each of them antibodies against these four different antigenic elements. Thus the close antigenic relation of our cultures to each other and to the original Panama strain is proved. Cross absorption tests confirmed this statement and showed, furthermore, that the three New York cultures do not possess any specific antigenic quality other than those present in the original Panama culture.

Conclusions as to the frequency of *Salmonella panama* in New York or elsewhere cannot be drawn from our limited material.<sup>8</sup> The occurrence in places as distant as Panama and New York and also the appearance in New York in two subsequent years, 1936 and 1937, suggest that it may be scattered over a larger area. Considering the particular serologic characteristics of our type, it is not unlikely that cultures occasionally have been mistaken for *Salmonella enteritidis* or *Salmonella aertrycke*. The special serologic character of the Panama type may sometimes even lead to the diagnosis paratyphoid A. Furthermore, our immunization experiments have shown that the original Panama culture as well as our own cultures contain an antigenic element which usually is encountered only in the group of *Salmonella supestifer*. Therefore, without knowledge of the Panama type, an erroneous diagnosis "supestifer" is possible.

For further studies as to the occurrence and significance of *Salmonella panama*, particular attention should be paid to infants. The literature of the last few years reports several outbreaks of diarrheas among

5. Amoss, H. L.: J. Exper. Med. 36: 25 (July) 1922. Kligler, I. J., and Olitzki, L.: Ztschr. f. Hyg. u. Infektionskr. 110: 459, 1929.

6. Voigt, O.: Monatschr. f. Kinderh. 23: 23 (April) 1922.

7. For furnishing these cultures I am grateful to the Bureau of Laboratories, Department of Health, New York City, Dr. F. Kauffmann, Copenhagen, and Dr. Gregory Schwartzman, Mount Sinai Hospital, New York.

8. Since this paper was written, another case has been found (July 1938, male infant 4 weeks of age, recovery).

infants in which "atypical" bacteria of the *Salmonella* group have been found.<sup>9</sup> As in Panama, however, adults may be affected.

Whether a systematic search would really reveal this type in other cases cannot be predicted, but it is almost certain that some other hitherto unknown or rare types of *Salmonella* will be discovered, once the modern methods of diagnosis are applied. Such experience has already been had by a number of investigators.<sup>10</sup>

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## HYPERTENSION A CENTURY AFTER BRIGHT

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One hundred and two years ago Richard Bright<sup>1</sup> first published his observations on the frequent coexistence of thickening of the arteries, cardiac hypertrophy and chronic renal disease. Finding no organic cause for the cardiac hypertrophy generally affecting the left ventricle, he said:

This naturally leads us to look for some less local cause, for the unusual efforts to which the heart has been impelled; and the two most ready solutions appear to be either that the altered quality of the blood affords irregular and unwanted stimulus to the organ immediately; or, that it so affects the minute and capillary circulation, as to render greater action necessary to force the blood through the distant sub-divisions of the vascular system.

Under the latter postulate Bright ascribed cardiac hypertrophy to increased peripheral resistance, which he believed was due to renal disease. It may therefore be said that he was the first to consider the renal origin of hypertension.

More specific reference to hypertension was made by Johnson,<sup>2</sup> who quoted Sanderson: "In cases of chronic Bright's disease with hypertension and hypertrophy of the left ventricle, the sphygmograph affords decided evidence of increased arterial pressure." Johnson emphasized the widespread arterial changes and expressed agreement with Bright that cardiac hypertrophy as well as diffuse vascular sclerosis was secondary to renal disease.

Gull and Sutton<sup>3</sup> confirmed Johnson's observations on small vessels and, impressed by the diffuse nature of the process, which they called "arteriocapillary fibrosis," they assumed that "these changes are, or may be independent of renal disease, and that the renal change in chronic Bright's disease with contracted kidneys, when present, is but a part of a general morbid condition." In thus concluding that diffuse vascular disease is a primary pathologic entity responsible for

increased arterial pressure, Gull and Sutton founded a school which stressed the nonrenal origin of hypertension, a teaching which has influenced accepted conceptions even to the present day.

Some ten years after the work of Gull and Sutton, von Basch<sup>4</sup> introduced the sphygmomanometer into clinical medicine and, as clinical measurements of blood pressure accumulated, it was only natural that attempts should be made to correlate hypertension with sclerotic changes in the blood vessels. However, exceptions to the rule soon appeared, and in 1893 von Basch,<sup>5</sup> after observing many cases of hypertension without demonstrable changes in the arteries, concluded that the elevation in blood pressure was but a precursor of arteriosclerosis. Huchard<sup>6</sup> in France and Allbutt<sup>7</sup> in England observed that organic disease of the arterioles was not sufficiently widespread to account for the increased peripheral resistance necessary to produce persistent hypertension in many patients. They expressed the belief that hypertension was primarily due to generalized vasoconstriction, which finally led to organic changes in the smaller vessels. There remained the question of what caused the vasoconstriction, but the kidney was not seriously considered as playing a major role in the production of this type of hypertension.

Up to the turn of the century there were three schools of thought concerning the interrelation of hypertension, arteriosclerosis and renal disease: (1) the followers of Bright, who believed that hypertension was due primarily to renal disease, (2) the followers of Gull and Sutton, who ascribed hypertension to widespread vascular disease and regarded the renal lesions as purely secondary, and (3) those who believed with Allbutt that hypertension was due to generalized vasoconstriction unrelated to renal disease.

A great advance in this field was made in 1904 by Jores,<sup>8</sup> who recognized two types of contraction of the kidneys, inflammatory and arteriosclerotic, and thus supplied the anatomic basis on which the clinician might distinguish nephritic hypertension. There remained, however, a much larger group of hypertensive patients in whom renal insufficiency rarely developed but who died of heart failure or a cerebral accident. Cases of this kind have been studied by many careful observers ever since the introduction of the sphygmomanometer into clinical medicine; they have been the source of much speculation as to the connection between arteriosclerosis, hypertension and renal disease—a controversy that has come down to the present time. The variety of terms used by past writers to designate the disease is evidence of the obscurity surrounding its nature. For example, Mahomed spoke of the pre-albuminuric state of chronic Bright's disease and von Basch of latent arteriosclerosis; Allbutt called it hyperpiesia, Janeway hypertensive cardiovascular disease and Volhard and Fahr benign and malignant sclerosis. In America it is most widely known as primary or essential hypertension.

Following the work of Jores and that of Volhard and Fahr,<sup>9</sup> both clinicians and pathologists recognized

9. Three cultures sent to me by Miss Beatrice McKinlay proved to be different from *Salmonella panama*. Fothergill, L. D.: *J. Infect. Dis.* 45: 393 (Nov.) 1929. Dulaney, A. D., and Michelson, I. D.: *Am. J. Pub. Health* 25:1241 (Nov.) 1935. McKinlay, Beatrice: *Infectious Diarrhea in the Newborn Caused by an Unclassified Species of Salmonella*, *Am. J. Dis. Child.* 54: 1252 (Dec.) 1937.

10. Hormaeche, E., and Peluffo, C. A.: *Arch. urug. de med., cir. y especialid.* 9: 673 (Dec.) 1937. Edwards, P. R.: *J. Hyg.* 36: 348 (July) 1936; *ibid.* 37: 384 (July) 1937. Topley and Wilson.<sup>3</sup>

From the Western Reserve University School of Medicine.  
Read before the Section on Practice of Medicine at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.

1. Bright, Richard: *Cases and Observations, Illustrative of Renal Disease Accompanied with the Secretion of Albuminous Urine*, *Guy's Hosp. Rep.* 1: 338, 1836.

2. Johnson, George: *On Certain Points in the Anatomy and Pathology of Bright's Disease of the Kidney; and secondly, on the Influence of the Minute Blood Vessels upon the Circulation*, *M.-Chir. Tr.* London 51: 57-78, 1868.

3. Gull, W. W., and Sutton, H. G.: *On the Pathology of the Morbid State Commonly Called "Chronic Bright's Disease with Contracted Kidney"*, *M.-Chir. Tr.* 55: 273, 1872.

4. von Basch, S.: *Ueber die Messung des Blutdrucks am Menschen*, *Ztschr. f. klin. Med.* 2: 79, 1881.

5. von Basch, S.: *Ueber latente Arteriosclerose*, Vienna, Urban & Schwarzenberg, 1893.

6. Huchard, H.: *Traité clinique des maladies du cœur et de l'aorte*, ed. 2, Paris, O. Doin, 1893, p. 892.

7. Allbutt, T. C.: *Diseases of the Arteries, Including Angina Pectoris*, London, Macmillan & Co., 1915, vol. 1.

8. Jores, L.: *Ueber Arteriosklerose der kleinen Organarterien und ihre Beziehungen zur Nephritis*, *Virchows Arch. f. path. Anat.* 178: 367, 1904.

9. Volhard, F., and Fahr, T.: *Die Brightsche Nierenkrankheit*, Berlin, Julius Springer, 1914.

that the kidneys of patients with essential hypertension were scarred as a result of more or less diffuse sclerosis of the smaller renal arteries, and the term nephrosclerosis was introduced to describe the condition.

However, in spite of the fact that pathologic changes in the renal vessels occur in a high percentage of cases of essential hypertension in which autopsy is done, there is still no uniformity of opinion regarding the relation of the kidney to hypertension. Indeed, most modern authors have departed so far from Bright's views as to conclude that the kidney is in no way concerned with essential hypertension. For example, in the latest edition of his book on hypertension and nephritis, Fishberg<sup>10</sup> expressed the commonly accepted view: "Essential hypertension is merely a collective concept for a number of conditions having in common the positive characteristics of arterial hypertension and the negative one of absence of primary renal disease," and regarding the pathogenesis of arterial hypertension he said "Hypertension, like fever, is merely a symptom and not a disease; sometimes hypertension is produced by renal disease, but more often it is not."

Space does not permit further discussion of the development of present day concepts of clinical hypertension, but they may be summarized as follows:

1. Hypertension of renal origin associated with obstruction of the urinary passages, glomerular nephritis, multiple cysts of the kidneys, periarteritis nodosa with marked renal involvement and severe renal amyloidosis. With clear evidence of renal disease in such cases, the renal origin of the associated hypertension is accepted by most workers in the field, although some (Kylin<sup>11</sup>) have denied that hypertension is ever caused by renal disease.

2. Essential hypertension is generally regarded as nonrenal in origin because (a) the systemic blood pressure is elevated in many cases for years before there is any demonstrable impairment of renal excretory function, (b) most patients with essential hypertension never show renal insufficiency but die of heart failure or a cerebral accident and (c) occasionally a patient with hypertension shows no anatomic evidence of renal arteriolar disease.

Let me now examine the foregoing arguments, usually advanced in support of the nonrenal origin of hypertension, in the light of the recent experimental observations of Goldblatt and his associates,<sup>12</sup> which indicated the role of the kidney in arterial hypertension.

Impressed by the frequency of arteriolar disease of the kidney in carefully studied cases of essential hypertension in human beings, and considering the possible functional effects of arteriolar sclerosis in causing progressive renal ischemia, Goldblatt in 1928 began his animal experiments designed to impair gradually the blood supply to the kidneys. Unable experimentally to produce narrowing of the million or more afferent glomerular arterioles, such as that in human arteriolar nephrosclerosis, he constricted the main renal artery by a special clamp so designed that any degree of narrowing up to complete occlusion of the vessel could be produced. He has shown that constriction of the renal artery of one kidney in both the dog and the monkey causes an elevation in the systolic and diastolic pressures which lasts for weeks or months, whereas narrowing of both renal arteries at once or after an interval results in persistent hypertension, which has continued in some animals for six years. The elevated blood pressure following the constriction of one renal artery promptly returns to normal on either removal of the ischemic kidney or release of the clamp on the artery—a crucial experiment illustrating the role of the kidney in raising blood pressure. Chronic hypertension is observed in animals that show no evidence of renal excretory insufficiency—the experimental counterpart of so-called benign essential hypertension in man. Also the picture of malignant hypertension with uremia, including widespread arteriolar necrosis, can be produced almost at will by further narrowing of the renal arteries. In other words, a dog with benign hypertension lasting for several years may be thrown into the malignant phase with uremic death in a few days, or the acute malignant phase can be produced in the beginning by severe constriction of both main renal arteries. In these experiments is seen the same baffling picture which has puzzled clinicians for the past hundred years, namely the occurrence of hypertension not only with but also without renal excretory insufficiency; yet the elevation of blood pressure in both instances is clearly of renal origin. Thus the argument that essential hypertension cannot originate from the kidney because there is often no accompanying impairment of renal excretory function is no longer valid.

The failure to find renal arteriolar disease in a few persons with essential hypertension is often cited as evidence that elevated blood pressure has nothing to do with the kidney, but the possibility of severe sclerosis of the main renal arteries sufficient to cause renal ischemia has not been excluded. Up to the present such cases have been overlooked and classified as instances of essential hypertension without renal arteriolar disease.

Although such recent workers as Fishberg<sup>13</sup> and Bell and Clawson<sup>14</sup> observed renal vascular disease in a high percentage of cases of essential hypertension, they did not consider the kidney as playing a major role in hypertension. For example, Fishberg in a study of seventy-two cases found renal arteriolar sclerosis in 100 per cent, while Bell and Clawson found renal arterial disease within the parenchyma of the kidney in 97.6 per cent and sclerosis of the afferent glomerular arterioles in 89.4 per cent of 420 cases of

10. Fishberg, A. M.: *Hypertension and Nephritis*, ed. 3, Philadelphia, Lea & Febiger, 1934.

11. Kylin, E.: *Ueber Hypertonie und Nierenkrankheit*, Zentralbl. f. inn. Med. **42**: 441 (June 4) 1921.

12. These observations have been reported in the following articles: Goldblatt, Harry; Lynch, James; Hanzal, R. F., and Summerville, W. W.: *Experimental Hypertension Due to Renal Ischemia*, Bull. Acad. Med., Cleveland **16**: 6, 1932.

Goldblatt, Harry; Lynch, James; Hanzal, R. F., and Summerville, W. W.: *Studies on Experimental Hypertension: I. The Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemia*, J. Exper. Med. **59**: 347 (March) 1934.

Goldblatt, Harry: *Studies on Experimental Hypertension: V. The Pathogenesis of Experimental Hypertension Due to Renal Ischemia*, Ann. Int. Med. **11**: 69 (July) 1937.

Goldblatt, Harry: *Studies on Experimental Hypertension: III. The Production of Persistent Hypertension in Monkeys (Macaque) by Renal Ischemia*, J. Exper. Med. **65**: 671 (May) 1937.

Goldblatt, Harry, and Kahn, J. R.: *Experimental Hypertension: Constriction of the Aorta at Various Levels*, J. A. M. A. **110**: 686 (Feb. 26) 1938.

Goldblatt, Harry; Gross, Jerome, and Hanzal, R. F.: *Studies on Experimental Hypertension: II. The Effect of Resection of Splanchnic Nerves on Experimental Renal Hypertension*, J. Exper. Med. **65**: 233 (Feb.) 1937.

Goldblatt, Harry, and Wartman, W. B.: *Studies on Experimental Hypertension: Effect of Section of Anterior Spinal Nerve*, Hypertension Due to Renal Ischemia, *ibid.*

Goldblatt, Harry, and Wartman, W. B.: *Studies on Experimental Hypertension: VII. The Production of the Malignant Phase of Hypertension*, *ibid.* **67**: 809 (May) 1938.

13. Fishberg, A. M.: *Anatomic Findings in Essential Hypertension*, Arch. Int. Med. **35**: 650 (May) 1925.

14. Bell, E. T., and Clawson, B. J.: *Primary (Essential) Hypertension: A Study of Four Hundred and Twenty Cases*, Arch. Path. **5**: 339 (June) 1928.



hypertension. In spite of these results, and after a critical survey of the problem, Bell and Clawson stated: "We do not have any theory of the etiology of primary hypertension to propose." On the other hand, Fahr, who has made an extensive study of renal arteriosclerosis, expressed the belief that hypertension is secondary to inflammatory as well as to arteriosclerotic renal disease. He called hypertension "compensatory" and of renal origin. The high incidence of renal vascular disease found post mortem in persons with hypertension is an established fact, but the role played by the kidney in the causation of hypertension has remained in controversy since Bright. The most recent work on the relation of arteriolar disease to chronic hypertension is that of Moritz and Oldt.<sup>15</sup> In a purely objective study of the arterioles from all parts of the body in 100 persons with and 100 persons without hypertension, they found a high correlation between arteriolar disease and hypertension in one situation only, the kidneys.

This century-old problem has now been elucidated by the experimental work of Goldblatt and his associates, which has been repeated and verified by many

tension frequently associated with natural or artificially induced menopause falls into this group. Hypertension of vasomotor and hence of nonrenal origin is associated with psychic disturbances. It also occurs in persons with increased intracranial pressure and in some with heart failure or with complete heart block.

Since arterial hypertension is a symptom and not a disease, its causes are varied, and any attempt to classify it is admittedly unsatisfactory. However, its origin as a symptom associated with certain disease states may be classified in the light of present knowledge, as shown in the accompanying table.

In classifying essential hypertension as of renal origin in the table, I am not unmindful of the limitations imposed in applying the results of animal observations to the problem of human hypertension, but in the face of such clearcut experimental results the risk of speculation is greatly reduced. Recalling Bright's conception of the relation between renal disease and the cardiovascular changes which he observed, I might have entitled this paper "Hypertension: Bright Vindicated."

All the experiments bearing on the pathogenesis of the hypertension induced by renal ischemia indicate that it is not of reflex nervous but of humoral origin. Some chemical substance circulating in the blood and formed as a result of renal ischemia constricts the peripheral arterioles and thus elevates the blood pressure. That a similar process may be involved in human essential hypertension is suggested by the work of Prinzmetal and Wilson<sup>16</sup> and of Pickering,<sup>17</sup> who have demonstrated that essential hypertension in man is not of vasomotor origin.

The experimental hypertension in animals without demonstrable evidence of renal excretory insufficiency is the experimental analogue of benign hypertension commonly seen in patients. Similarly, when the renal arteries of these animals are still further constricted uremia develops with extensive retinal lesions, and post-mortem examination shows arteriolar necrosis like that observed in malignant hypertension in man. For the production of arteriolar necrotic lesions in the animal two factors are essential, (1) hypertension and (2) progressive renal insufficiency—the same combination that always occurs in the malignant phase of essential hypertension in man. Much light is thus thrown on the cause of such lesions, and it is no longer necessary to invoke toxic agents such as lead, syphilis and rheumatic fever to explain them.

Whether the hypertension associated with primary renal disease also results from renal ischemia is a problem for the future to disclose, but it is likely that such disease of the kidney may so alter its circulatory dynamics that the functional effects on systemic blood pressure may be the same as in primary vascular disease.

Although Goldblatt's work throws no light on the nature of human arteriosclerosis, it goes far in clearing up the problem of hypertension, which has baffled clinicians for decades. It is now possible to understand why patients exhibiting sclerotic changes in the vascular system may or may not have arterial hypertension: If the renal vessels are sufficiently involved in the process, hypertension appears; if they are spared, the patient

Clinical Hypertension

RENAL	NONRENAL
1. Essential hypertension	1. Endocrine disturbances
2. Primary renal disease	(a) Basophilic adenoma of the pituitary
(a) Glomerular nephritis (acute and chronic)	(b) Adrenal tumor
(b) Pyelonephritis	(c) Hyperthyroidism
(c) Urinary obstruction	(d) Menopause
(d) Periarthritis nodosa of renal vessels	(e) Obesity
(e) Polycystic renal disease	2. Vasomotor disorders
(f) Severe amyloidosis of kidney	(a) Increased intracranial pressure
3. Coarctation of the aorta?	(b) Psychic disturbances
4. Eclampsia?	(c) Circulatory failure
	(d) Complete heart block

workers both here and abroad. Certain it is that their observations afford the first clear proof of the renal origin of essential hypertension. It appears that his renal arterial clamp produces the same effect on systemic blood pressure in the animal that renal vascular disease produces in the human being.

CLINICAL HYPERTENSION

We may now consider hypertension in human beings in the light of the facts available from animal experiments, under two headings: (1) renal and (2) nonrenal. In the first group falls that hitherto obscure condition of a large number of persons, called primary or essential hypertension. Here also belongs primary renal disease, i. e. glomerular nephritis, pyelonephritis from urinary obstruction, multiple cysts of the kidneys, periarthritis nodosa of the renal vessels and renal amyloidosis in some cases. The hypertension observed in cases of coarctation of the aorta may also be of renal origin, since clamping of the aorta above the renal arteries in the animal causes cephalad hypertension, whereas similar narrowing of this vessel below the renal arteries has no effect on the blood pressure. In group 2 are included hypertension associated with endocrine disorders, such as basophilic adenoma of the pituitary and rare adrenal tumor. The systolic hyper-

15. Moritz, A. R., and Oldt, M. R.: Arteriolar Sclerosis in Hypertensive and Nonhypertensive Individuals, *Am. J. Path.* 13: 679 (Sept.) 1937.

16. Prinzmetal, Myron, and Wilson, Clifford: The Nature of the Peripheral Resistance in Arterial Hypertension with Special Reference to the Vasomotor System, *J. Clin. Investigation* 15: 63 (Jan.) 1936.  
17. Pickering, G. W.: The Peripheral Resistance in Persistent Arterial Hypertension, *Clin. Sc.* 2: 209 (May) 1936.

may show no significant elevation in blood pressure and survive to a ripe old age, in spite of widespread arteriosclerosis elsewhere in the body. Furthermore, it now appears that the clinical course pursued in hypertension is determined primarily by the progress of the vascular disease in the kidneys. This in the majority of cases is sufficient to cause chronic hypertension, but not rapid enough to impair renal excretory function. Thus most hypertensive patients die of heart failure or of a cerebral accident before uremia develops. However, the renal vascular changes may progress to a point where the excretory function of the kidney is impaired, when the clinical picture of so-called malignant hypertension with uremia appears. In other words, the progress and extent of vascular disease in the kidneys determine whether essential hypertension runs a benign or a malignant course.

The shadows hitherto surrounding the pathogenesis of essential hypertension are gone, and with them the necessity for the use of such terms as primary or essential. With more assurance than ever before, physicians may now regard such hypertension as a symptom of renal vascular disease.

#### SUMMARY

The most plausible explanation of the increase in arterial pressure exhibited by patients with so-called primary or essential hypertension is, in the light of Goldblatt's recent work on experimental hypertension, as follows: Arterial and arteriolar sclerosis of the renal vessels leads to renal ischemia, which by a humoral mechanism produces an increased muscular tone in the peripheral arterioles and thus causes elevation in the systemic blood pressure.

City Hospital.

#### ABSTRACT OF DISCUSSION

DR. T. HOMER COFFEN, Portland, Ore.: Yesterday I had the privilege of seeing at the Lane Medical Library in San Francisco a volume entitled "Report of Medical Cases," published by Richard Bright in 1827. The color engravings are still as clear and bright as they were when they were published. The first eighty-eight pages not only describe cases clinically but include exact postmortem observations. His speculations as to the cause of dropsy are shown in the following: "One great cause of dropsical effusions appears to be obstructed circulation. Whatever either generally or locally prevents the return of the blood through the venous system gives rise to effusions of sera more or less extensive; thus diseases of the heart which delay the passage of the blood into the venous system give rise to general effusion, both into the cavities and into the cellular tissue. An obstruction to the liver, by causing a delay in the passage of the blood through the veins connected with the vena portae, gives rise to ascites." He further states "There are other appearances to which I think too little attention has been paid. They are evidences of organic changes which occasionally present themselves in the structure of the kidneys and which, whether they are to be considered as the cause of the dropsical effusion or as the consequence of some other disease, cannot be unimportant." Bright lived seventy-five years before the use of the sphygmomanometer and so knew nothing of arterial hypertension. He and his two contemporaries Hodgkin and Addison must have had many discussions about the patients they saw in Guy's Hospital, where Bright often spent from four to six hours a day. Bright's observations still stand as landmarks in the still unsolved riddle of what we today call essential hypertension. Following the clinical use of the sphygmomanometer about three decades ago, the whole question of the relation of kidney disease to arteriosclerosis, arterial hypertension and cardiac disease has been speculated on and is still unsolved. At

the beginning of the century there were three schools of thought; first, Bright's followers, who thought the condition was primarily renal; second, the followers of Gull and Sutton, who thought the condition was due to widespread vascular damage; and, third, those who thought that the condition was largely due to vasoconstriction. While Goldblatt's work is most significant as to the effect of the kidney in producing hypertension, much remains in the way of investigation to determine what factors are concerned in this phenomenon.

DR. FRANK R. NUZUM, Santa Barbara, Calif.: Dr. Scott's paper weighs the evidence and concludes that the most constant morphologic expression of essential hypertension is disease of the renal arterioles. He believes that the results of Goldblatt's experimental work can be applied to essential hypertension in human beings and concludes that arteriosclerosis of the kidney vessels, leading to renal ischemia, is essential in the elevation of the systemic blood pressure. My associates and I have approached this problem by making an accurate determination of kidney function of persons with essential hypertension and comparing the results with those obtained in normal persons of the same age groups. On a group of 212 hospitalized private patients, careful studies of renal function were conducted, in each instance under identical conditions. A Volhard concentration and dilution test was done on the third day of bed rest. Following this procedure, phenolsulfonphthalein and urea clearance tests were done. From this group the data of 100 purely essential hypertensive patients were taken for critical analysis of laboratory results. These observations were compared with a group of twenty-five patients with chronic valvular heart disease, excluding hypertension, all compensated and with no gross evidence of edema, and with forty normal persons. Each of the groups was divided into decades. The average percentage of phenolsulfonphthalein excretion from decade to decade was approximately 12 less in the hypertensive group than in the normal group. The heart group was intermediary. The urea clearance test gave an average clearance of 60 per cent for the hypertensive group, an average clearance of approximately 75 per cent for the normal group, and about the same reading for the heart group. In the Volhard test, the six hour elimination of urine, after ingestion of 1,000 cc. of fluid, averaged for the hypertensive group 683 cc., for the heart group 882 cc. and for the normal group 823 cc. The average excretion of night urine was 300 cc. for the normal group and about 450 cc. for the hypertensive group. The heart patients were again intermediary but approximated the normal persons quite closely. The average concentrating ability of the patients with hypertension as determined by this test was 1.019. For the normal group the figure was 1.023, and the heart group in this instance was almost exactly midway. From this brief summary it is evident that the renal function of the hypertensive group was less efficient than that of the controls or even that of chronic heart patients without hypertension or edema. Even though these tests were done as accurately as possible and special means were taken to make them accurate, renal function tests of this kind are after all not sensitive, and it is possible that a more delicate test would indicate that kidney function is more disturbed than these grosser tests indicate. If such an interpretation is proper, this discrepancy between the kidney function in normal persons and in those with hypertension would be widened. The interpretation of these results is not as simple as might appear off-hand.

DR. R. W. SCOTT, Cleveland: One of the chief difficulties in associating essential hypertension with the kidney has been the fact that most hypertensive patients never develop renal excretory insufficiency and, as I indicated in the paper, this problem is now elucidated by Goldblatt's experiments which show clearly that marked hypertension from renal ischemia may exist for years without renal excretory insufficiency. Finally, I would point out that Goldblatt's observations suggest that the kidney may be concerned in the maintenance of normal blood pressure, which if true will be even a more important contribution than the light his experiments have thrown on the problem of hypertension.



in chemical action long enough for the flesh wound to heal would seem to be of some advantage. Dr. Irwin Danielson of the Biochemical Department of the University of Oklahoma School of Medicine has carried out several chemical experiments with the magnesium alloys in an attempt to retard or alter their action in the tissues. The metal will take a chemical coating of silver or nickel, which slows its action in sodium phosphate solution, but the coating film prepared to date does not have the desired mechanical features when placed in the tissues. It will not take an electrolytic

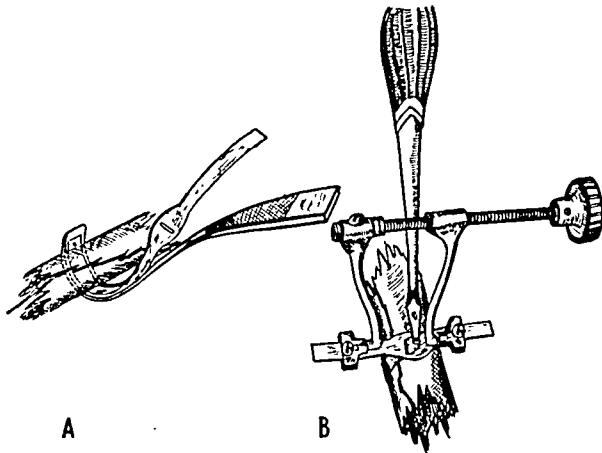


Fig. 3.—Method of using magnesium-manganese band similar to Parham band. A, instrument for passing band around the fragments. B, an instrument for tightening the magnesium alloy band. A small screw fastens the band to the cortex and the loose portion of the ends of the band are cut off with scissors.

plate of nickel or silver satisfactorily but the plate formed does seem to reduce the rate of early chemical solution of the metal in vitro. Magnesium, manganese and aluminum are electropositive, falling just below calcium in the electromotive series. The electrolytic action can easily be demonstrated by the ammeter method of Venable and Stuck<sup>14</sup> in their work on the electrolytic action of metals. Even though this action occurs it causes no obstacle to the use of the metal and may even be an advantage, since there is a stimulation of periosteal proliferation and callus formation followed by gradual absorption of the metallic substance.

#### DESIGN OF APPLICATION

**Screws and Pegs.**—The design of the head and the thread count of the magnesium screw have been found to be important.<sup>15</sup> Experiments showed that more rapid erosion of the screw takes place at the neck and head, a point at which the greater concentration of serum salts can come in contact with the metal. The head is now made but slightly larger than the body of the screw and tapered so as to be countersunk in a reamed out bed in the drill hole. It is then covered with bone wax. The threads on the screw are now made coarser, twenty-four to the inch, for security. The screws may be any size, long or short, but no greater quantity of magnesium should be used than is necessary, and the screws are selected which will penetrate the cortex on both sides of the shaft, yet no larger than are necessary for strength. A great advantage is that the

screws can be easily cut to any length by a bone cutting forceps.

For an eight to twenty-four thread screw a drill, size 30, is used and threads are made by a threader tap corresponding to the size of the screw. The hole is reamed out with the corner of a small chisel deep enough to countersink the screw head flush with the surface of the cortex. Bone wax is pressed over the head of the buried screw.

The magnesium pegs may be any size from that of a tiny pin to that of a good size nail. Their shafts should preferably be three cornered.

When one inserts the screw the fragments should be held well immobilized with the drill holes of both fragments in line; otherwise the screw will bind and twist off before it is entirely sunk.

**Slotted Plates.**—The very thin sheet magnesium and manganese alloy may be used in the form of a plate by placing one edge in a longitudinal saw cut slot across the fracture line and bending enough of the plate down on the cortex to be fixed with screws. There are instances in which the bone fragments must be held in firm alignment following operation, yet something lighter and more temporary than the heavy conventional steel plate is desirable for the immobilizing agent. The fragments are reduced and fixed with clamps while the saw cut is made across the fracture line. A piece of metal is cut with scissors, wide enough so that half of its width may be inserted edgewise into the saw cut and the other half bent over the cortex where holes are suitably drilled. The screws should extend through both sides of the cortex. It is of considerable advantage to be able to cut the metal with the scissors to any desired size or shape and to drill the holes at arbitrary points. Hawley<sup>16</sup> has recently described the efficiency of this mechanical principle.

**Circular Band.**—The Parham band often fulfils a distinct need in selected cases, especially in oblique, comminuted or butterfly fragments. Magnesium alloy cannot be fastened exactly as a Parham band because it will break quickly if bent backward over the slot in the conventional manner and pressed down flatly. It will withstand a very strong tension if not kinked. Therefore, the band is designed so that each end may be pulled on and fixed with a screw. A special instrument is devised for application.

**Medullary Peg.**—The metal has been used in several instances as a small medullary peg and, contrary to Hey Groves's experience with rabbits, no undue effects were experienced. The absorption is slower than when the metal penetrates the cortex, and a marked stimulation of periosteal proliferation occurs.

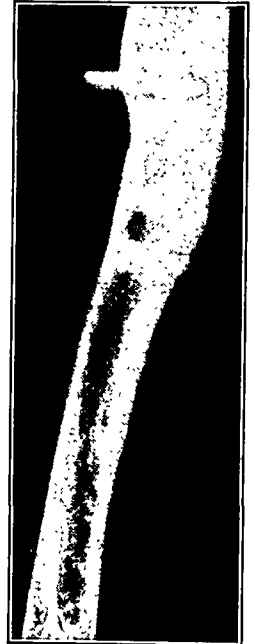


Fig. 4.—Beef bone screws sometimes do not absorb for several years, while magnesium alloys absorb in a few months. Appearance two and one-half years after onlay bone graft with beef bone screws still unabsorbed.

14. Venable, C. S.; Stuck, W. G., and Beach, Asa: The Effects on Bone of the Presence of Metals Based upon Electrolysis, *Ann. Surg.* 105: 917-938 (June) 1937.

15. The alloy metal was obtained from the Dow Chemical Company and the Aluminum Company of America.

16. Hawley, G. W., and Padula, R. D.: A Bone Plate Which Will Not Break or Bend, *J. Bone & Joint Surg.* 20: 469-472 (April) 1938.

## SELECTION OF CASES

In general those cases must be selected in which the smallness in size of the alloy metal screws and pins will suffice in rigidity and strength and where they will serve to good mechanical advantage. Devices made of harder metals may be better depended on in the heavier bone shafts, but many fractures require only a single nail or screw for satisfactory fixation, and such an agent might be more willingly employed if it could be depended on to absorb readily.

The alloy screws have been used in six cases of onlay bone graft. All have held firmly and absorption of the metal left the graft thoroughly amalgamated and the fragments firmly united. The stimulation of osseous callus was notable in each case.

## ACTION OF MAGNESIUM ALLOY ON THE TISSUES

*Systemic Effect.*—There has been no systemic symptom observed in any of the cases in which magnesium metal was employed. Since the metal dissolved with the formation of magnesium salts, which are not known to be toxic, there need be no apprehension in this respect.

*Effect on Periosteum and Bone.*—Magnesium produces a marked proliferation in the periosteal tissue and deposit of osseous callus in the region of its insertion,

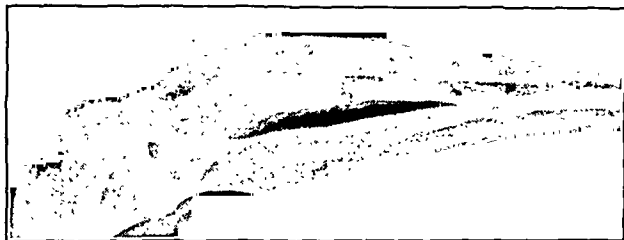


Fig. 5.—Magnesium alloy screws absorbed in six and one-half months.

but the screw hole, when examined after absorption of the metal, retains the original thread impressions and shows virtually no change in the cancellous tissue. The x-ray examination often gives the impression of cystic bone, but operation has proved that gas and not a cystic formation produces this appearance. Magnesium, manganese and calcium stimulate enzymes and phosphates in bone. An extraordinary phenomena in one experiment on dogs is worthy of special attention: A magnesium-aluminum alloy wire the size of a Kirschner wire was passed through the skin and bone without an incision being made, and extensive periosteal proliferation rapidly occurred symmetrically throughout the entire length of the bone shaft. This gives rise to the possibility of producing periosteal proliferation in cases of deficiencies, nutritional deformities and cystic degeneration of bone.

*Effect on Articular Tissue.*—There is no reaction shown in articular cartilage except that which is produced from the trauma of penetration.

*Microscopic Effect.*—There is no inflammatory reaction in the tissues adjacent to the absorbing metal. Small gas cysts may be seen with separation of muscle bundles, and there is a certain amount of increase of serum. There is a granulation area about the screw but the absorption of bone is very slight. There is evidence of marked proliferation of fibrous tissue and calcification.

## CHEMICAL AND BIOLOGIC FATE OF THE METAL

*Absorption Rate.*—1. The rate of absorption depends on the size and quantity of metal used. A 1 Gm. screw of 95.7 per cent magnesium, 4 per cent aluminum and 0.3 per cent manganese placed in the humerus was completely absorbed in 120 days after insertion.

2. The metal is attacked more actively in traumatized bone tissue or softened bone fragments than in hard cancellous bone.

3. The absorption rate varies with the extent to which the serous fluids have access to the metal substance. Screws removed ten weeks after insertion in the ulna showed a thin layer of granulation tissue extending from the periosteal surface downward surrounding the metallic substance. The screw was more greatly absorbed at its neck at the surface of the cortex. The screw was still firm deeper in the hard cancellous bone. The head of the screw lying on the wound side of the cortex was more greatly eroded than the point lying in undisturbed tissue on the opposite side of the cortex.

## EVOLUTION OF GAS

A gas is demonstrable in the roentgenogram within two or three days after insertion of the magnesium metal through a fractured bone. Starting with a slight shadow at the head of the screw there will appear several areas of gas within the first ten days. Other writers mention this gas as being hydrogen. It is true that, when magnesium is placed in salt solutions, hydrogen is rapidly given off. However, the gas drawn from pockets in the tissues, on several occasions, has proved to be chiefly nitrogen. Hydrogen absorbs quite as rapidly as it forms, while nitrogen is slow to absorb and may form gas pockets and press toward the periphery. An analysis by Dr. Danielson of gas aspirated forty days after application of a band of magnesium alloy showed: carbon dioxide 5.6 per cent, oxygen 6.5 per cent, hydrogen 7.3 per cent and nitrogen 80.6 per cent.

The tendency for the gas to pocket varies with the extent to which the metal is exposed to the attack of the blood serum. If the oxidation is slow, as it is when the metal is well buried in hard cortical bone, the gas absorbs about as rapidly as it forms. If the reaction is too rapid the gas may form a fluctuating subfascial pocket. Simple puncture or aspiration has left no complications.

## SUMMARY

The magnesium alloy containing magnesium 95.7 per cent, aluminum 4 per cent and manganese 0.3 per cent is acceptable for use as bone screws or pegs. The metal maintains fixation of bone fragments long enough for them to unite yet gradually absorbs completely in a much shorter time than other absorbable materials commonly used.

The phenomenal stimulation of periosteal proliferation bears future study for possibilities in osteomalacia, delayed union and nutritional deformities.

The effervescence of a gas during the process of oxidation of the metal is objectionable but not a contraindication to its use. It is rapidly absorbed and is no more harmful than so much air in the tissues.

The behavior of this metal in bone is favorable enough to encourage its limited use, and further biochemical studies may disclose other very valuable properties.

717 North Robinson Street.

## ABSTRACT OF DISCUSSION

DR. CHARLES SCOTT VENABLE, San Antonio, Texas: I find myself opposed to Dr. McBride's estimation of the value of magnesium alloys in bone surgery. It is admitted that magnesium alone is not suitable for bone surgery, so that to make it sufficiently rigid it is alloyed with aluminum and manganese, making three components of widely different electrical potential, aluminum heading the list of baser metals in the law of electromotive force of metals. My associates and I have shown through a long series of animal experiments that the electrolytic action between metals in bone, which applies equally to a single crew of different components, is not only present in vivo but is the cause of local decalcification, with in many instances the overstimulation of fibroblasts which Dr. McBride has described, which in turn become osseous, forming excess callus. It is only when a metal is entirely passive or electrically neutral to the moisture in which it is placed that no electrolytic action is present. This is true of all metallic compounds or alloys except one of cobalt, chromium and molybdenum, which is and remains passive. It is called vitallium. The passivity of a metal is due to the fact that it contains and retains a molecular veil, which protects it from the fluid or moisture above it. Oxidation is the third quotient in this process. A metal may become passive if it is in such a fixed position that the molecular veil which forms about it cannot be wiped off by motion. However, such stillness is not insurance that this phase will be so in all instances. As Dr. McBride has said, magnesium alloy screws must not be used with steel plates. This is because electrolytic action is again greatly magnified and the results rather disastrous. We have used this with the magnesium with the Dow metal as well as with other metals. It may be actively demonstrated in either blood serum or salt solution. Dr. McBride has pointed out that the head and shank of a magnesium screw deteriorate much more rapidly if left beyond the cortex than when countersunk and covered with bone wax. Naturally so, because the movement of tissue over the head prevents the formation of a molecular veil and hence no passivity of the metal is acquired, while that part of the screw engaged in the bone may become passive. The mechanical weakness which Dr. McBride described is an important consideration, for one must be able to trust a metal not to break. This applies also to the thin sheet of magnesium-manganese alloy which he described as being very malleable and soft but at the same time unfortunately breaking when crimped.

DR. J. ALBERT KEY, St. Louis: It is obvious that the magnesium alloy is a very severe irritant to bone and that it causes absorption of bone that is in contact with it. After the bone and the soft tissues have been insulted by an operation I consider it bad surgery to add to the insult by generating gas at the site of the operation and I cannot conceive of gas accumulating in tissues to the extent that it looks like a cyst and yet not forming pressure. So I think magnesium is a very dangerous material to put in operatively wounded bone.

DR. EARL D. MCBRIDE, Oklahoma City: There is much to be said against magnesium and I have realized it from the start. Verbrugge in Antwerp did quite a lot of work on it. I was attracted by his work and I thought I would try it out. I have found that it can be used and that it is not unsafe. As Dr. Key says, one should be cautious about any material that is acknowledged to be more or less an irritant, but the irritation from it does not last very long. It suffices to carry out the fixation, and if we develop the right mental attitude toward it, giving it credit for its advantage as well as its disadvantage, some good may come out of it. I certainly would not advise its whole-hearted adoption at the present time. Dr. Venable said he has a metal devised to create no irritation and I have one that I am studying that creates some irritation but does just the opposite of his metal; it absorbs and gets out of the way. I think there are some good uses to come from this metal.

MALIGNANT NEOPLASMS OF THE  
NASOPHARYNX

I. JEROME HAUSER, M.D.

DETROIT

AND

DURWIN HALL BROWNELL, M.D.

ANN ARBOR, MICH.

It was sixteen years ago that Gordon New called the attention of the medical profession to malignant neoplasms of the nasopharynx. He stressed the fact that the regional metastases, vague symptoms referable to one ear or diplopia, and not the primary lesion, bring the patient to the physician. Between that time and 1931 he reported almost 250 cases of nasopharyngeal malignant growths which he had studied. In spite of his complete and adequate description of the syndrome, as well as dissertations by Quirk and Cutler, Beck and Guttman, Christensen and McArthur, Ewing, Ferreri and many others, it appears that general practitioners, and even otolaryngologists, are still not well enough acquainted with malignant lesions of the nasopharynx to recognize them during their early stages.

Within recent years an opportunity of studying a series of such cases has been afforded the Department of Otolaryngology at the University of Michigan Medical School. The majority of these patients had been in the hands of general practitioners and some of them had been seen by otolaryngologists without receiving a correct diagnosis. In several instances surgical procedures had been undertaken to alleviate the symptoms without recognition of the primary lesion in the nasopharynx.

It is because we believe that carcinoma of the nasopharynx is a relatively common disease, one which the general practitioner should suspect and the otolaryngologist diagnose with ease, that we are prompted to review and emphasize again a group of symptoms and signs which often lead to the correct diagnosis. Further, we shall also attempt to show that all epithelial neoplasms arising from the lining membrane of the nasopharynx are medullary squamous cell carcinomas and that it is not necessary to employ such terms as lympho-epithelioma and transitional cell carcinoma.

## CLINICAL MATERIAL

The diagnosis of malignant neoplasm of the nasopharynx has been made in fifty cases in this department during the past ten years and in every instance this diagnosis was confirmed by biopsy. Forty-six cases were called carcinoma, three were diagnosed as lymphoblastoma and in one instance the lesion was a myeloma.

In reviewing this series, the initial complaint was listed in every case and on several occasions it was necessary to list two separate complaints, for they appeared concurrently. Twelve patients described swelling of the neck as the first symptom, while ten had aural pain or a full sensation referred to one ear, eight complained of headaches or pain in the ear and eight more had pain in the throat as the initial symptom. Six of them complained first of pain in the face, while numbness of the face, facial paralysis and diplopia were original complaints in three others. The diagnosis of the one case of myeloma of the nasopharynx was made in a patient who had no symptoms referable to the ears, nose or throat.

Read before the Section on Laryngology, Otolaryngology and Rhinology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 17, 1938.



Analysis of the patients' illness before the establishment of the diagnosis of malignant neoplasm of the nasopharynx revealed that a majority of them had noted a cervical swelling or had symptoms referred to one ear or pain in the ear, while a few had nosebleeds, nasal obstruction or sore throats. Seven complained of double vision and five had noted a unilateral loss of vision.



Fig. 1.—Section of biopsy specimen showing an adenocarcinoma, supposedly arising in a teratoma.

Pain or numbness of the face was the complaint of several more, and two patients had a drooping of one eyelid while two had noted a facial paralysis.

On objective examination there were palpable nodes in the necks of more than half of the fifty patients. Discoloration of the tympanic membrane, fluid in the ear or a discharging ear was found in twenty-one of the patients. A unilateral paralysis of the sixth nerve was observed in nine cases and in three additional cases the paralysis was bilateral. Hypesthesia of one side of the face was also found and seven patients had some

TABLE 1.—Initial Complaints

Cervical swelling.....	12
Ear symptoms.....	10
Headaches, pain in head.....	8
Pain in throat.....	8
Nasal obstruction.....	6
Epistaxis.....	4
Pain in face.....	2
Numbness of face.....	1
Facial paralysis.....	1
Diplopia.....	1
No otorhinolaryngologic complaint.....	1

degree of optic atrophy. Five patients had a paralysis of the superior oblique muscle and four had evidence of oculomotor paralysis. In three patients there was a facial paralysis and in three others drooping of the upper eyelid. Two subjects showed evidence of vagus nerve paralysis and two others had unilateral hypoglossal involvement. In one patient there was a complete unilateral nerve deafness as well as a glossopharyngeal paralysis. One subject showed a Horner's syndrome and another, with a chronic mastoiditis, had a typical Gradenigo syndrome.

The duration of symptoms before the correct diagnosis was made varied from the time when the neoplasm was found on routine otolaryngologic examination up to five years. In the average case a little over one year elapsed from the onset of symptoms until

the final diagnosis was made. In addition to numerous paracenteses 32 per cent of the patients had had some type of surgery performed before the diagnosis of malignant neoplasm of the nasopharynx was established.

Roentgenograms of the skull were not taken as a routine diagnostic measure, although such films were made on many occasions and frequently showed involvement of the sphenoid sinus, invasion of the mastoid or petrous ridge or destruction of the base of the skull.

A diagnosis of carcinoma was made in forty-six of the cases under observation and in the great majority

TABLE 2.—Analysis of All Symptoms

Cervical swelling.....	24
Symptoms referable to one ear.....	23
Discharging ear.....	5
Headache, pain in head.....	17
Epistaxis.....	9
Nasal obstruction.....	9
Sore throat, pain in throat.....	9
Diplopia.....	7
Pain in face.....	5
Loss of vision.....	5
Numbness of face.....	4
Facial paralysis.....	2
Drooping of eyelid.....	2

of instances it was called an undifferentiated medullary squamous cell carcinoma. On three occasions the diagnosis was adenocarcinoma and we believe that one of these arose in a teratoma, for it was directly in the midline and almost filled the nasopharynx. It occurred in an 18 year old girl who complained of nosebleeds of six months' duration. The bleeding was apparently more marked at the time of menstruation and the patient was sent to us with the diagnosis of vicarious menstruation. The neoplasm was first treated by irradiation, followed by excision and two and one-half years has now elapsed since the tumor was removed with no sign of recurrence.

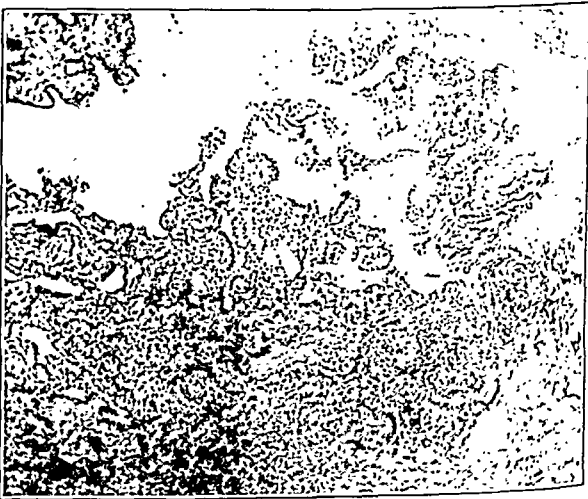


Fig. 2.—Section of adenocarcinoma arising in the left fossa of Rosen müller.

One of the other adenocarcinomas occurred in a man aged 54 who complained of a cervical swelling for one year. A biopsy of the gland revealed a poorly differentiated adenocarcinoma, while examination of the nasopharynx showed a serosanguineous discharge coming through the ostium of the left sphenoid. The sphenoid was opened and the primary lesion found. In spite of local radium therapy to the sinus and external irradiation to the neck, he had widespread metastases two months later.

The third adenocarcinoma was found in a 47 year old woman who came to us Oct. 18, 1937, complaining of nasal obstruction. She presented an ulcerated obstructive lesion arising in the left fossa of Rosenmüller and partially filling that side of the nasopharynx. She received extensive radiation therapy but the lesion has not completely disappeared.



Fig. 3.—Section of carcinoma of basal and prickle cell type.

There was one case in which the neoplasm was a carcinoma of a mediocellular type with a somewhat pseudo-adenomatous architecture and this occurred in a woman aged 54, who complained of pain in her left ear, lasting four months. The primary lesion was very small and was located in the left fossa of Rosenmüller, and the patient had a unilateral external rectus paralysis. Although intensive irradiation therapy was used,

TABLE 3.—Objective Signs

Cervical swelling.....	28
Changes in tympanic membrane, discharging ear.....	21
Unilateral sixth nerve paralysis.....	9
Bilateral sixth nerve paralysis.....	3
Trigeminal nerve involvement.....	7
Optic atrophy.....	7
Trochlear nerve paralysis.....	5
.....	5
.....	5
.....	5
Vagus nerve involvement.....	2
.....	1
.....	1
.....	1
Gradenigo's syndrome.....	1

there was a progression of symptoms and increase in size of the neoplasm within ten months.

Still another carcinoma was of the basal and prickle cell type. It occurred in a man aged 71 who had noticed swelling of the cervical glands for a year and had had a sanguineous discharge from the right ear for six months. After the diagnosis was made he did not return for treatment.

One carcinoma was diagnosed as a pseudo-adenomatous basal cell carcinoma. Occurring in a man aged 60 who complained of pain in the right side of the head persisting for ten months, the neoplasm arose in the right fossa of Rosenmüller and partially filled the right side of the nasopharynx. The lesion was accompanied by paralysis of the second, third, fourth, fifth and sixth cranial nerves on the right side and the last

time we saw the patient, six months after the completion of intensive irradiation, there was a marked increase in the size of the neoplasm.

There was also one case of cornifying squamous cell carcinoma occurring in a man aged 55 who suffered from a persistent sore throat, stuffy sensation in the head and deafness. In addition to the primary lesion in the nasopharynx there were cervical metastases, and ten months after external irradiation was completed this patient was still free from recurrence.

One carcinoma, in a woman 50 years of age, developed in an adamantinoma. Five months before consulting us she complained of a numbness of the face, and two months after that she began to notice loss of vision. The tumor filled the nasopharynx and eroded the base of the skull with invasion and destruction of the sella turcica. The growth was partially removed by an intracranial operation, but at the present time, six months after the operation, there is extensive recurrence.

In the remaining cases the diagnosis was medullary squamous cell carcinoma, either B 3 or B 4, and in many cases the neoplasm was so undifferentiated that considerable study of the sections was necessary before the tumor could be called a carcinoma rather than sarcoma, although in no instance was it deemed necessary to call the neoplasm a lympho-epithelioma or transitional cell carcinoma.

TYPICAL CASES

CASE 1.—A man aged 56 complained three years earlier of decreased hearing and stuffy sensation in the right ear. He was treated with ear drops but the symptoms progressed and two months before consulting us extraction of the teeth failed to give relief. About the same time he noticed a weakness of the right side of the face and a swelling in the right side of the neck for which he was given three roentgen treatments. Six weeks



Fig. 4.—Section of cornifying squamous cell carcinoma.

after this the right ear began to discharge and on the day preceding his consultation with us a right mastoidectomy was advised. Examination showed a right complete peripheral type of facial palsy, and there was an odorless serous exudate in the right external auditory canal. The tympanic membrane was purple red and moderately full, with an anterior inferior marginal perforation. A walnut-sized lymph node in the right side of the neck was considered neoplastic. Biopsy of the right side of the nasopharynx showed a medullary carcinoma, B 3, and roentgenograms of the skull demonstrated extensive osteoblastic metastases to the base of the skull on the right side.

In spite of intensive irradiation to the nasopharynx, neck and base of the skull, he died after thirteen months.

**CASE 2.**—One patient, a girl aged 19, first noticed enlarged glands in the left side of the neck eight months prior to consulting us, and a short time later a tonsillectomy was performed on her. The swelling in the neck progressed, and three months before coming to us enlargement of the right cervical nodes was observed. She had received three roentgen treatments to the neck as well as ultraviolet irradiation, and examination showed firm, discrete, bean-sized nodes along the posterior cervical chain on each side. There was a smooth constructive lesion in the left side of the nasopharynx, the biopsy showing a highly undifferentiated carcinoma. She was given intensive irradiation to the nasopharynx and both sides of the neck. At the completion of the roentgen treatments she complained of pain in the left arm, and roentgenograms of this arm showed a metastatic lesion involving the junction of the middle and proximal thirds of the humerus. Palliative irradiation to the involved area was administered but metastases rapidly developed in the right femur, right scapula and spine, with death ensuing less than one year after the diagnosis was made.

**CASE 3.**—A man aged 30 complained of pain and stiffness of the right side of the neck some three months prior to consul-

disappearance of the lesion. Recurrences developed locally in the cervical nodes, however, and she died eight months after the diagnosis was made.

Of the four malignant neoplasms of the nasopharynx which were not called carcinoma, one was a myeloma of the plasmocytoma type:

**CASE 5.**—A man aged 53 came to the University Hospital complaining of alternating constipation and diarrhea of one and one-half years' duration. An annular lesion of the rectum was found, and biopsy revealed myeloma of the plasmocytoma type. Though he had no symptoms referred to the head or neck, in routine examination in the otology clinic a walnut-sized, round, nonulcerating lesion involving the orifice of the left eustachian tube was found and there were palpable nodes on each side of the neck. Biopsy of the lesion in the nasopharynx revealed exactly the same type as that in the rectum. He did not receive therapy at this hospital.

The three remaining cases were diagnosed as lymphoblastoma. A typical case is as follows:

**CASE 6.**—A man aged 45 complained of left sided headache of six months' duration. He stated that he had had a bloody discharge from his nose for twenty-five years and that eighteen years before this consultation a growth had been removed from the nasopharynx. Examination showed the right tympanic membrane to be discolored and somewhat full, and there was increased tissue about the mouth of the eustachian tube on this side. Biopsy of this tissue revealed a poorly differentiated neoplasm, a lymphoblastoma. He was given prolonged radiation therapy to the nasopharynx with disappearance of the lesion, and five months later local recurrence was not evident but there were symptoms suggesting intracranial extension.

#### PATHOLOGY

In reviewing the literature on nasopharyngeal carcinoma, one finds such terms as lympho-epithelioma and transitional cell carcinoma, in addition to the names commonly applied to malignant neoplasms arising from squamous epithelium. In the study of the slides of our own cases it has appeared to us that it is not necessary to employ such special terms and that the group is adequately described by the term medullary squamous cell carcinoma.

Some mucous membrane surfaces are covered by stratified squamous epithelium consisting of delicate cells with no spines, no keratin and little capacity to cornify. This type of epithelium covers the tonsils, the vault of the pharynx, the nasal passages, the base of the tongue and the nasopharynx. Tumors arising from such epithelium present microscopic and clinical peculiarities which have led many investigators to classify them as a special variety of epidermoid or squamous cell carcinoma. Such neoplasms do not produce bulky growths but metastasize early to regional lymph nodes, often making the enlarged nodes the first sign of the disease. These tumors show cells which are small, are uniform in size, and have scanty cytoplasm and large hyperchromatic nuclei. They infiltrate the submucosa or lymphoid tissue singly, in solid groups or in anastomosing columns. In the metastases the cells may reveal some traces of squamous character or they may become even more undifferentiated, their structure suggesting lymphoblastoma.

Regaud and Schminke first employed the name lympho-epithelioma in speaking of certain tumors arising from mucous membrane surfaces, because they believed that the lining membrane of the nasopharynx, lying over lymphoid tissue, was so altered as to give rise to a particular form of carcinoma. Such tumors are characterized by the failure of the epithelial cells



Fig. 5.—Section of a highly undifferentiated carcinoma arising in the nasopharynx.

tation with this department. A tonsillectomy failed to relieve his symptoms and one month after the onset of the pain he developed swelling of the cervical glands, at the same time suffering occipital headaches, which persisted at the time he came to us. Examination of the nasopharynx showed increased tissue in the vault and there were hard nodes in each side of the neck. Biopsy of the nasopharynx and cervical nodes showed a squamous cell carcinoma, and although he was treated with intensive radiation therapy he died one year later.

**CASE 4.**—Four months before coming to us, a girl aged 14 years complained of a left earache, and following a paracentesis the ear drained continuously. She also complained of loss of hearing in the left ear and for two months had constant frontal headaches, numbness and pain in the left side of the face, and double vision. Examination revealed decreased hearing in the left ear, a left external rectus paralysis, weakness of the trigeminal nerve and left twelfth cranial nerve paresis. The tympanic membrane on the involved side was dull, thickened, injected and bulging. There was no discharge from the ear, but there were small palpable nodes in each side of the neck and examination of the nasopharynx revealed a tumor mass surrounding the orifice of the left eustachian tube. A biopsy of this mass was reported as an undifferentiated medullary carcinoma. Roentgenograms of the base of the skull showed clouding of the left mastoid with questionable destruction of the floor of the left middle fossa. She was given intensive irradiation with

to assume squamous characters, the cells remaining undifferentiated.

The term transitional cell carcinoma likewise implies a modification, that the neoplasm lacks characteristics of ordinary squamous epithelium. Epithelium capable of giving rise to this type of carcinoma is said to line certain portions of the larynx, trachea, esophagus and especially the ducts of the mucous glands. It is believed that when this epithelium undergoes malignant change it is capable of giving rise to a special form of carcinoma.

Although it has been suggested that some nasopharyngeal carcinomas may arise from embryonal cells, there is actually little or nothing to support this contention.

Stedman's medical dictionary defines lympho-epithelioma as "a malignant epithelioma of the rhinopharynx, tonsils and pharynx, arising from the lymphoid tissue of the pharynx." To us this definition appears illogical, for according to all basic conceptions of the origin of malignant neoplasms an epithelioma can arise only from epithelial tissue.

It is our impression that so-called lympho-epitheliomas and transitional cell carcinomas are highly anaplastic carcinomas. We have been unable to perceive changes in the nasopharyngeal epithelium occurring as a result of its proximity to lymphoid tissue. We believe that the epithelium of the nasopharynx, normally lacking in spines, keratin and ability to cornify, in undergoing malignant degeneration must of necessity give rise to a highly anaplastic neoplasm. Furthermore, if one is willing to call such tumors highly undifferentiated carcinomas, the group becomes an all inclusive one with nothing in the cellular detail justifying special terminology.

Because of the marked radiosensitivity of carcinomas of the nasopharynx, certain scientists have argued that they should be classed as a special type of carcinoma. We believe that these tumors are radiosensitive because of their structure—no keratin, no cornification, very little cytoplasm and but little connective tissue between the cells. The radiosensitivity does not characterize the tumor but is the result of the character of the tumor, of the particular micro-anatomic structure that exists in practically all malignant neoplasms arising in the nasopharynx.

#### COMMENT

As our data imply, symptoms referable to the nasopharynx may be entirely absent. The tumor, arising in the fossa of Rosenmüller or in the vault of the nasopharynx, may have attention called to it not because of its local existence but rather as a result of extension to the adjacent tissues, or metastases. Cervical metastases occur early in the disease, undoubtedly because of the highly anaplastic nature of the neoplasm.

Any person, regardless of age, with a persistent cervical swelling, should have a careful examination of the nasopharynx and biopsy of any suspicious appearing tissue. There may be early erosion of the base of the skull or invasion of the sphenoid sinus, with resultant headaches. Consequently it becomes a highly desirable practice to examine in a routine manner the nasopharynx of every patient who suffers unexplained headaches. Unilateral deafness or a full sensation in one ear should always cause the examiner to look at the orifice of the eustachian tube, irrespective of whether or not he is thinking of carcinoma. When the tympanic membrane is somewhat hemorrhagic, the fossa of Rosenmüller should be inspected with the greatest of care. A

discharging ear, with exudate that is serous or sero-sanguineous for more than a few days and especially if the tympanic membrane has a purplish red discoloration, is suggestive of carcinomatous invasion of the eustachian tube or mastoid, while frequently the invasion of this tube, or the occlusion of the opening by the neoplasm, results in the first symptom.

Diplopia or paralysis of the rectus lateralis muscle, coming on gradually or suddenly, should suggest a nasopharyngeal carcinoma, and paralysis of any one or several cranial nerves demands inspection of the nasopharynx. When the objective examination is not conclusive, roentgenograms of the sphenoid sinuses may give additional information.

#### TREATMENT

The treatment of this disease, in our experience, is unsatisfactory. External irradiation of the local lesion is the usual procedure, from 200 to 400 roentgens daily through several ports, the dose being carried to skin tolerance, and it is usually given over a period lasting

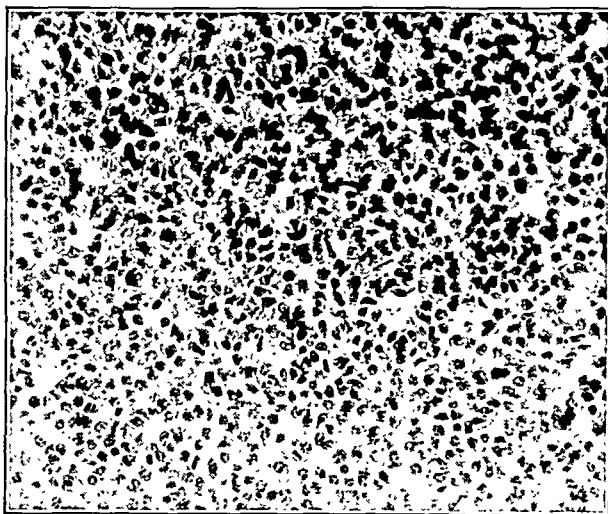


Fig. 6.—Section of biopsy specimen of nasopharynx showing a poorly differentiated neoplasm, a lymphoblastoma.

from four to six weeks. Instances of cervical metastases were similarly irradiated. In a few isolated cases, following external irradiation, radon seeds were implanted in the local lesion, and in two instances in which there was involvement of the sphenoid sinus the sinus was opened and a radium capsule placed in it until 2,500 mg. hours of irradiation had been given. Yet, in spite of radiation therapy as intensive as we could administer it, only three patients of this series are free from carcinoma a year and a half after diagnosis. One patient, treated nineteen months ago, does not show any neoplasm; one patient suffering from adenocarcinoma arising in a teratoma is free after two and one-half years, and one patient is free of recurrence after eight and one-half years.

Even though these results have been most unsatisfactory, it appears that earlier diagnosis would result in a better prognosis. A consciousness on the part of all physicians for neoplasms of the nasopharynx and familiarity with symptoms and signs which suggest such a lesion would probably lead to an early tentative diagnosis, while careful routine inspection of the nasopharynx by the otolaryngologist might uncover many neoplasms which otherwise remain long unrecognized.

## CONCLUSIONS

1. Malignant neoplasms of the nasopharynx often manifest themselves by symptoms which are extranasal in nature.

2. Cervical swellings, changes in the tympanic membrane, unilateral deafness or stuffy sensation in one ear, pain in the head or throat, diplopia or rectus lateralis paralysis, or unilateral paralysis of any cranial nerves calls for careful examination of the nasopharynx.

3. All malignant neoplasms arising from the lining epithelium of the nasopharynx appear to be medullary squamous cell carcinomas. Lympho-epithelioma and transitional cell carcinoma are believed to be highly undifferentiated forms of squamous cell carcinoma.

4. Irradiation is at present the only form of treatment. In spite of poor results, if earlier diagnoses were made, chances of arresting or destroying the neoplasm would be greater.

5. The nasopharynx should be given careful routine inspection by the otolaryngologist.

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## ABSTRACT OF DISCUSSION

DR. JOSEPH C. BECK, Chicago: I wish the authors could have presented all of their paper, because there are practical points in it which they did not have time to read. I am going to take the liberty of bringing some of those points out. New called attention to the smallest type of neoplasm and yet a large lymphatic mass on the side of the neck, a metastasis. These small neoplasms occur in the nasopharynx, somewhere around the ostium tube or just behind it. The patient complains of headache; there may be an abducens paralysis, and many symptoms are noticed. In that small space where the tumor is located there may be so many nerves involved that it is not surprising to find the multiplicity of symptoms. The radiologist makes those growths disappear in the neck as well as the postnasal space. Often even if treated the patient has metastasis in the long bones or in the abdomen. I have seen that happen repeatedly. The authors showed one case of an epidermoid type of carcinoma in the postnasal space. That is rare; also the adenocarcinomas, which are very resistant to treatment with radium or x-rays, are not frequent. It is difficult in many cases to examine the nasopharynx and it is not convenient. Many times if one cocaineizes the patient's pharynx and retracts the palate one will be surprised to find a small neoplasm, and at that time radiologic treatment (not surgical, although surgery is often wrongly employed) may save these patients. I cannot see anything in the surgical treatment of this type of tumor, whether by surgical diathermy or the cold method. If anything will do any good, it is radium and x-rays, but the tumors should be irradiated before these multiple symptoms arise. The authors find fault with the classification. They say we should call them just cancer or medullary carcinoma. I think Schmincke and others who have studied the histopathology want to stick to the transitional type of epithelium class because it is a type that histologically can be shown and it is highly radiosensitive; but, after all, as the authors say, they all fit into a stage of medullary epithelium. They find objection to the lymphoid epithelioma classification. Many others will find that same objection. Why should one expect a lymphatic cell to be transformed into a carcinoma cell? It is an entirely different family of cells; that was some one's dream which was widely spread in the literature and I hope it may be expurgated soon.

DR. JOHN H. CHILDBREY, San Francisco: Unless these growths are diagnosed and treated early, death occurs, on the average, seven months after correct diagnosis. The authors have shown that when the patient comes with symptoms the disease is far advanced, as the result of the activity of the lesion and of mistakes in diagnosis. The latter may be avoided by routine examination of the nasopharynx in all patients for these hidden tumors. The examination is not

easy without practice, and the many negative examinations try the rhinologist's patience. However, although they are infrequent, sooner or later a tumor is discovered. The three cranial nerves that are particularly apt to be affected by lesions of the nasopharynx are the sixth, fifth and ninth, in that order. The sixth cranial nerve in Dorello's canal is immediately adjacent to the body of the sphenoid, and the ganglion of the fifth lying on the petrous is a lateral relation to the sixth. Involvement of these two nerves indicates a tendency of the carcinoma to extend upward, forward and laterally from the nasopharynx to the petrous tip. Therefore it may be advisable, because of the bone intervening between the petrous tip and the cavity of the nasopharynx, not only to irradiate the nasopharynx from within and through the temporal region but also to open the sphenoid as the authors did and insert radium into the cavity of the sinus, thus getting closer to the lesion and its extensions and thus insuring a more thorough irradiation of the malignant growths. About one half of the grade 3 or 4 squamous cell epitheliomas and lymphosarcomas of the tongue and of all the pharyngeal cavities are primary in the nasopharynx. Of malignant tumors of the nasopharynx, the commonest is the highly malignant grade 4 squamous cell epithelioma. Eighty per cent of these nasopharyngeal growths occur in males. Although the average age of patients so affected is 44 years, both epithelioma and lymphosarcoma occur in patients under 20 years of age and in fifteen cases the average age was 14 years. In 42 per cent of cases, cervical metastasis is the first symptom noticed. Lymphosarcomas of the nasopharynx are correctly diagnosed sooner than squamous cell lesions because the former are larger and obstructive symptoms pointing to the nasopharynx occur sooner. Involvement of cranial nerves occurs oftener from epithelioma than from lymphosarcoma. With regard to treatment, these patients must be under the observation of a laryngologist and a radiologist for one or two years.

DR. ROBERT F. RIDPATH, Philadelphia: I wish to discuss another kind of malignant tumor of the nasopharyngeal space which has not been mentioned—the chordoma. There have been very few chordomas reported, principally because they have not been recognized. A chordoma is a malignant tumor arising from the notochord, increasing in size, destructive in nature, so much so that it not only destroys the base of the skull but invades the sphenoidal area, going into and destroying the ethmoidal labyrinth and extending into the maxillary antrum. The symptoms are slightly different from those of the ordinary malignant growth found in this particular neighborhood. Usually it arises from a trauma of some kind. This trauma, however, may have been of some years' duration, so that the proliferation or the growth is slow in nature. The two patients who came under my observation were struck in the region of the head some two years before this growth was recognized. The growth extends in all directions, upward, forward and downward, increasing in size and bulging out into the epipharyngeal space. There are two or three peculiar things about it. It is malignant without any metastasis. Note the point "without any metastasis." Also blindness quickly develops, paralysis quickly develops and there are nausea, vomiting and bleeding not only from the mouth but also from the nose.

DR. JAMES F. PERCY, Los Angeles: Comparatively speaking, I see many nasopharyngeal malignant growths in my cancer service at the Los Angeles County Hospital and I generally see them after everybody else has got through with them. The statement was made in the discussion that these patients are never surgical. I think they are always surgical, but not with the cold steel knife. I have time merely to mention what I do with the actual cautery in their surgical treatment. The first step is a bilateral block dissection and ligation of the external carotid arteries by the method of Dawbarn, published in 1903. This surgeon did not tie these arteries by a single ligature as is usually done but also tied and sectioned all the branches bilaterally. If the growth can be felt with the finger in the postnasal region, I section the soft palate with the cautery knife and apply my ball tipped cautery, inside a water-cooled jacket, and completely destroy the mass. If

too much good tissue is destroyed, including bone, nature will fully care for it in the final healing. If I am not sure that I have reached the limits of the growth by the oral route, I make a horseshoe shaped incision through the face and enter the antrum. From this vantage point any part of the nasopharynx can be reached and the cancer area infiltrated with heat. Local recurrences are rare because the cautery leaves a surface on which it is difficult for cancer to redevelop. I have many of these cases, usually terminal, in which the patients are alive and free from morbidity years afterward, and especially after plastic surgeons have had a chance to improve what the disease and the cautery may have taken away. Preoperative and postoperative irradiation is not the answer to the treatment of cancer in this location except possibly in a small percentage of minor cases or for palliation. The actual cautery (not diathermy) as it can be used today offers more for the life and happiness of the cancer patient than does any other method.

DR. BARNEY M. KULLY, Los Angeles: I wish to discuss the question of a thorough examination of the nasopharynx. Perhaps there is no place in our field that we examine so poorly as we do the nasopharynx. Most of us rely on a postnasal mirror. It isn't always possible to use a postnasal mirror, and sometimes in the stress of a busy practice we are apt to overlook an examination when we are unable to examine a patient with a mirror. Even in the cases in which we can see the nasopharynx with a mirror we are seeing a much foreshortened image. It is like trying to see the face of a thirteen story building from the sidewalk below it. The next method is the Holmes nasopharyngoscope, but with the Holmes instrument the image we see is at right angles to the instrument and consequently there is a blind spot directly ahead of the instrument that we cannot see. The most effective method of examining the nasopharynx is by pulling the palate forward and looking at it directly either by the method of Dr. Beck, using a catheter, or by the direct nasopharyngoscope of Yankauer. This is a trumpet-like instrument with a handle on it. This instrument is slipped back of the palate usually without anesthesia. It can be done in every patient. It can be handled in the nasopharynx as is a laryngoscope in the larynx. Structures can be pushed aside, the fossae of Rosenmüller examined and even the anterior lip of the eustachian tube visualized. I do not mean that this method should be used to the exclusion of other methods, but in every case in which there is the least doubt a direct speculum should be inserted and an examination made. In what was probably a meningocele of the nasopharynx seen through this instrument there was a bulging mass in the nasopharynx, found on direct examination. It had the appearance of a smooth walled cyst or abscess. Before this was opened it was painted with iodine and aspirated. The return was a clear cerebrospinal fluid. There was no untoward sequela. I believe this represented a meningocele through a patent craniopharyngeal duct.

DR. I. JEROME HAUSER, Ann Arbor, Mich.: A word about treatment in our own place: With the one exception of the adenocarcinoma arising in a teratoma, we have treated all these neoplasms with irradiation alone. Patients were given external radiation to the nasopharynx through two or three ports, daily, often for from four to six weeks. Where there were cervical metastases they were likewise treated intensively with daily doses of from 200 to 400 roentgens. In general our results have not been good. We have only three patients who are living after one and one-half years. I have had no experience with the hot cautery or the soldering iron in this location. We must respect Dr. Percy's results, because of his experience and because his patients are living and ours are not. I think it matters little whether we call these lymphosarcomas or call them highly undifferentiated carcinomas. I am certain that many of the cases that we are calling highly undifferentiated carcinomas would be in the hands of other pathologists lymphosarcomas, and many that they call lymphosarcomas we would call carcinoma. The important thing is to recognize the lesion early and get after it just as intensively as we know how to do it.

## Clinical Notes, Suggestions and New Instruments

### A CASE OF QUARTAN MALARIA FOLLOWING TRANSFUSION AND TREATED WITH SULFANILAMIDE

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NEW YORK

Transfusion of whole blood has become a commonplace in clinical therapeutics within the last two decades. As a rule, steps are taken to exclude syphilis in the donor. Little attention is ordinarily paid to other infectious diseases. A number of cases wherein diseases other than syphilis are alleged to have been transmitted to patients through the medium of transfusion have been reported. Of these malaria is the most important, especially in regions where malaria is prevalent. Since 1911, when Woolsey<sup>1</sup> reported the first accidental transmission of malaria as the result of blood transfusion, numerous case reports have appeared, particularly from countries where malaria is not common, and transfusion seemed to be the only likely source of infection. In many cases the parasites have been identified in the blood of the donor. Wright<sup>2</sup> has recently made a thorough review of the subject, and has collected twenty-nine cases from the literature which have been described in sufficient detail to warrant acceptance of transfusion as the medium through which the malaria was transmitted.

Another case herewith described has recently been studied in the Presbyterian Hospital:

#### REPORT OF CASE

T. R. C., a housewife aged 30, American born of Italian parentage, admitted to the surgical service of the Presbyterian Hospital Jan. 6, 1938, complained of a painful swelling in the left lower costal region of two months' duration.

The patient was a native of Hazelton, Pa., and had never been more than 100 miles from this town. Her past history was uneventful, except that at the age of 18 some "swollen glands" had been removed from the right side of her neck.

Beginning in June 1937 she began to suffer from "heart burn," nausea, night sweats and fatigue. In November she began to have pain in the left lower anterior portion of the chest, shortly followed by a tender swelling at the same site. The swelling slowly increased and the pain persisted during the following two months. The pain was not increased by respiration. There was no cough, sputum, fever or chills. One week before admission this swelling was aspirated and 20 cc. of sterile pus was obtained. During this seven months of illness her weight gradually dropped from 125 pounds to 100 pounds (57 to 45 Kg.).

On admission the rectal temperature was 100 F. The pulse rate was 104, and the respiratory rate 24. Near the anterior axillary line on the left lower part of the chest wall was a smoothly rounded, slightly tender swelling about 4 cm. in diameter. Aside from a well healed surgical scar along the anterior edge of the right sternocleidomastoid muscle, physical examination was negative. The spleen and liver were not felt.

The laboratory data were as follows: Blood count: hemoglobin 72 per cent (Sahli); red blood cells 4,270,000; white blood cells 5,040; polymorphonuclear leukocytes 69 per cent, lymphocytes 22 per cent, mononuclears 8 per cent, eosinophils 1 per cent. The smear was negative. Urinalyses were negative. A tuberculin test was positive. Stereoscopic roentgenograms of the chest showed "shadows in both apexes probably tuberculous in origin." The remaining lung fields were clear. Roentgenograms of the abdomen showed a well visualized splenic shadow which was of "about normal size."

During her first five days in the hospital, her temperature range was from 99 to 100.4 F.

A diagnosis of cold abscess was made, and on January 11 the patient was operated on under avertin with amylene hydrate

From the Department of Medicine, Columbia University College of Physicians and Surgeons, and the Presbyterian Hospital.

1. Woolsey, G.: Transfusion for Pernicious Anemia: Two Cases, *Ann. Surg.* 53: 132, 1911.

2. Wright, F. H.: Accidental Transmission of Malaria Through the Injection of Whole Blood, *J. Pediat.* 12: 327 (March) 1938.



and cyclopropane anesthesia. At operation, the abscess was excised. The walls of the abscess showed lesions characteristic of tuberculosis.

Because of her postoperative weakness and pallor, it was decided to give her a transfusion. On January 13 she was given a direct transfusion (multiple syringe method) of 600 cc. from her husband. One hour later she had a shaking chill, lasting for twenty minutes, with a temperature of 102.6. During the following four days her temperature ranged from 99 to 101. On January 18 she was given a second 600 cc. transfusion (same method), this time from her brother-in-law. After this transfusion her temperature rose to 104 but she had no chill.

She remained in the hospital until February 5. During this period her temperature varied between 99 and 102.8 F., with a general downward trend. At this time no cause for the fever was found, aside from apical infiltration. January 24 the white blood cells numbered 7,880 with polymorphonuclear leukocytes 67 per cent, lymphocytes 26 per cent and mononuclears 7 per cent. No abnormal cells were reported on the smear.

February 5 the patient left the hospital and returned home. She did not feel well, however, and complained of chilly sensations. February 10 she had the first of a series of severe shaking chills, with fever to 103 or 105 F. The initial chill occurred twenty-eight days after her first and twenty-three days after her second transfusion. The chills recurred at regular intervals of three days during the next three weeks. During this time there was no cough, production of sputum or pain in the chest.

March 4 she was admitted to the Presbyterian Hospital for the second time, this time to the medical service. On this admission her temperature was 102.8, with a pulse rate of 100 and a respiratory rate of 20. Eight hours after admission her temperature rose to 105. The patient was acutely ill with hot, moist skin and definite pallor. The recent operative scar was well healed. The lungs were clear. Examination of the abdomen disclosed a large, firm, tender spleen which descended 6 cm. below the costal margin. The liver was down 2 cm. The remaining observations were negative.

Examination of the blood revealed hemoglobin 69 per cent, red blood cells 3,510,000, white blood cells 4,800, polymorphonuclear leukocytes 73 per cent, lymphocytes 24 per cent and mononuclears 3 per cent. The smear showed *Plasmodium malariae* gametocytes and ring forms. The sedimentation rate was 73 mm. in one hour. The remaining observations were negative.

Having established the diagnosis of quartan malaria, it was decided to try the effect of sulfanilamide. Typical malarial chills had occurred March 4 and 7, with a rise of temperature to 105 on each occasion and large numbers of quartan parasites in the blood. March 9 the patient was started on sulfanilamide by mouth in doses of 0.9 Gm. every six hours. March 10 a chill occurred at the expected hour with a peak temperature of 104 F. Parasites continued to be present in the circulating blood on this date and through March 12. March 13, the date of the next expected chill, no chill appeared, and no parasites were demonstrated in the blood.

March 14 the patient was given a transfusion of 600 cc. of citrated blood from a new donor. Immediately after 600 cc. had been given a chill occurred and the temperature rose to 104.6 F. This chill occurred eighteen hours after the calculated time for a malarial chill and was quite similar to the chill that followed her first transfusion. No plasmodia were demonstrated after this chill.

Meanwhile, sulfanilamide was being continued in doses of 3.6 Gm. a day. This dose was continued for seventeen consecutive days (March 9 to 26). No toxic symptoms from sulfanilamide were observed.

Following the post-transfusion chill the temperature ranged from 98 to 100 F. No subsequent chills occurred, and repeated blood smears were negative for plasmodia. During this period the size of the spleen steadily diminished, being barely palpable April 16. Her sense of well-being increased and her weight rose from 84 pounds to 94 pounds (38 to 42.6 Kg.). Additional chest films showed no change.

After sulfanilamide was stopped, March 26, the temperature curve showed no change during the following twenty-one days.

April 11, sixteen days after sulfanilamide was stopped, the patient was given 0.5 cc. of 1:1,000 epinephrine subcutaneously. After ten minutes thick smears were made of venous blood and examined for malarial parasites. None were demonstrated.

#### COMMENT

The origin of this patient's malaria was obviously from one of three sources; i. e., a lighting up by the operation of an old malaria of which the patient had no recollection, or transmission through transfusion from one of the two donors. With regard to the first possibility, the patient had always lived in Pennsylvania, where quartan malaria is practically nonexistent.<sup>3</sup> She had never had symptoms suggestive of malaria. The spleen at the time of operation was not enlarged. It is unlikely that a latent malaria would be reactivated four weeks after, instead of at the time of, operation. The likelihood that this patient had had a previously latent malaria therefore seems remote. It was tentatively assumed that the patient had acquired the infection from one of the antecedent blood transfusions.

The donor of the second transfusion was 38 years old. He was born in the interior of central Italy. He stated that he had never had malaria. At the age of 13 years he came to this country, lived near Hazelton, Pa., for about five years and then moved to New York City, where he had lived ever since. He had never been south of Pennsylvania. His spleen was not palpable. He would not submit to the injection of epinephrine but allowed 20 cc. of blood to be removed from his vein. The blood was defibrinated and concentrated by centrifugation according to the method of Bass and Jones,<sup>4</sup> and thick smears were made of the top layers. No malarial parasites were found in his blood. There seemed to be no reason to suspect him of being the source of the patient's infection.

The donor of the first transfusion was 38 years old. In 1920, while in Albania with the Italian army, he had had malaria, with the chills occurring every third day. He was treated with quinine in February 1921. Immediately thereafter he came to the United States, settling in Hazelton, Pa., where he had lived ever since. He had made brief trips to Baltimore and Washington but had never been farther south. Since his treatments with quinine seventeen years before, he had had no chills or fever. On examination his spleen was not palpable. His blood was examined several times for malarial organisms. On one occasion 1 cc. of 1:1,000 epinephrine was administered subcutaneously, and after ten minutes he noticed palpitation, tremor, weakness and giddiness. At this time 50 cc. of blood was withdrawn from his vein and concentrated and examined by the method already described. No malarial parasites were found in the blood of this donor.

It is recognized that malarial parasites, especially of the quartan variety, can remain latent in the internal organs of the body for prolonged periods. Jankelson<sup>5</sup> reported a case of quartan malaria in a 6 weeks old infant transmitted by the intramuscular injection of blood from the father, who had had malaria thirty-seven years previously in Italy. The parasites were still demonstrable in the father's blood. Naveiro<sup>6</sup> observed a patient who had quartan malaria which was transmitted by the transfusion of blood from a donor who had had no symptoms of malaria for thirty-seven years. McCulloch<sup>7</sup> described the case of a woman in Toronto who contracted quartan malaria following transfusion from a donor who had had malaria in Rumania twenty-five years before and had had no symptoms of the disease in the interim. Wright<sup>2</sup> described an infant (case 3) in whom malaria developed four weeks after transfusion from the father, who had been free from symptoms of malaria for thirty-three years.

There is, then, good reason to believe that malarial parasites might well remain hidden in small numbers within the body of the first donor and that through the stimulus of transfusion

3. Boyd, M. F.: *An Introduction to Malariology*, Cambridge, Mass., Harvard University Press, 1930.

4. Bass, C. C., and Jones, F. M.: *The Cultivation of Malarial Plasmodia (Plasmodium Vivax and Plasmodium Falciparum) in Vitro*, J. Exper. Med. 16: 567, 1912.

5. Jankelson, I. R.: *Transmission of Malaria Through Injection of Whole Blood*, J. A. M. A. 97: 177 (July 18) 1931.

6. Naveiro, R.: *Paludismo por transfusión sanguínea*, *Semana méd.* 1: 1588 (May 24) 1934.

7. McCulloch, E.: *Quartan Malaria Transmitted by Transfusion*, *Canad. M. A. J.* 37: 26 (July) 1937.

sufficient parasites could be liberated so as to infect a susceptible individual, although present in such small numbers as to be overlooked by the ordinary methods of detection.

The incubation period between transfusion and the appearance of the first malarial chill has varied between twenty-four hours<sup>1</sup> and forty-nine days<sup>8</sup> in other reported cases and has been as long as one year in a case of artificial inoculation with an attenuated tertian strain.<sup>9</sup> In the case here reported the incubation period between the patient's first transfusion and her first chill was twenty-eight days, which represents a fair average of other reported cases.

We believe that this represents a case of quartan malaria transmitted by blood transfusion, because of the lack of other possible sources of infection and because of the clearcut history of malaria of the same type in the first donor seventeen years previously, this period of latency of the disease in the donor not being incompatible with his being a carrier of malarial parasites.

Malaria has been treated with sulfanilamide by others. Van der Wielen<sup>10</sup> in the Netherlands had reported its first use in this condition in June 1937. He noted that in a patient with dementia paralytica, who was being treated by fever therapy with quartan malaria, the chills ceased and plasmodia temporarily disappeared from the blood following the use of sulfanilamide for an intercurrent cystitis. The dose of sulfanilamide was 0.3 Gm. three times a day for eleven days. Exemplifying the wisdom of Pasteur's dictum concerning "chance and the prepared mind," he attempted to substantiate this finding by giving sulfanilamide to a second patient with dementia paralytica under treatment with quartan malaria. In the second case the dose of sulfanilamide was increased to 0.6 Gm. three times a day and was continued for twenty-one days. In this case, both fever and plasmodia permanently disappeared.

Working independently, Díaz de León,<sup>11</sup> in Mexico, reported in October 1937 the successful use of sulfanilamide in the treatment of fifteen patients with spontaneous tertian malaria. He used oral doses of 0.6 Gm. three times a day for an unspecified number of days.

A third independent observation was recorded by Hill and Goodwin<sup>12</sup> in Georgia, who noted the complete elimination of the tertian parasite while a patient was being treated for hemolytic streptococcal infection with prontosil.<sup>13</sup> On the basis of this observation and of Van der Wielen's results, Hill and Goodwin used prontosil in seven cases of tertian and in ninety-three cases of estivo-autumnal malaria. Prontosil was given intramuscularly in doses of 10 cc. every twelve hours for four or (rarely) more injections. The drug was successful in every case.

We believe that sulfanilamide has been effective in curing the case of malaria reported here. The termination of the three day cycle of chills and fever, the disappearance of parasites from the circulating blood, the diminution in size of the spleen and the clearcut clinical improvement all followed in logical sequence after the administration of sulfanilamide.

The effectiveness of sulfanilamide in combating a protozoan infection, in addition to its now well established potency against the beta-hemolytic streptococcus is of great theoretical as well as practical importance. The mode of action is not proved but a direct toxic effect of sulfanilamide on the parasite is suggested.

#### SUMMARY

1. A tuberculous patient apparently acquired quartan malaria by transfusion of blood one month previously from her husband, who had had an attack of quartan malaria seventeen years before.

8. Stein, H. B.: Transmission of Malaria by Transfusion: Report of a Case with Two Acute Developments of the Disease When Blood from the Same Donor Was Used, *Am. J. Dis. Child.* 44: 1048 (Nov.) 1932.

9. Mayne, B.: Protracted Incubation in Malarial Fever: Report of a Case and a Review of the Literature, *Pub. Health Rep.* 52:1599 (Nov. 12) 1937.

10. Van der Wielen, Y.: "Prontosil" in Quartan Malaria, *Nederl. tijdschr. v. geneesk.* 81: 2905 (June 19) 1937.

11. Díaz de León, Amonario: Treatment of Malaria with Sulfonamide Compounds, *Pub. Health Rep.* 52: 1460 (Oct. 15) 1937.

12. Hill, R. A., and Goodwin, M. H., Jr.: "Prontosil" in Treatment of Malaria, *South. M. J.* 30: 1170 (Dec.) 1937.

13. Prontosil is the disodium salt of 4-sulfamido-phenyl-2'-azo-7'-acetyl-amino-1'-hydroxynaphthalene-3', 6' disulfonic acid.

2. The malaria was apparently cured by sulfanilamide, as witnessed by the termination of chills and fever, the disappearance of parasites from the circulating blood, the shrinkage of the spleen and the definite clinical improvement.

3. On the basis of this case and the literature cited, it is suggested that sulfanilamide be tried in a large series of cases of malaria.

70 East Seventy-Ninth Street—622 West 168th Street.

#### ACTUAL SITE IN SKIN OF INTRADERMAL INJECTION

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There is a quite general belief that an intradermal injection to be properly given must be injected into the epidermal layers of the skin. It is considered that the typical "bleb" which results from such an injection represents a division of the epidermal layers of the skin. When this is not accomplished the procedure is considered incorrectly performed.

The fallacies of injection into the deeper layer of the skin (corium) have been repeatedly pointed out. In figure 1 are shown diagrams taken from two recent discussions. On the left is indicated the "correct" method of intradermal injection with the needle point plainly in the epidermal layer. On the right is shown the "wrong" site of injection with the needle beneath the epidermal layer.

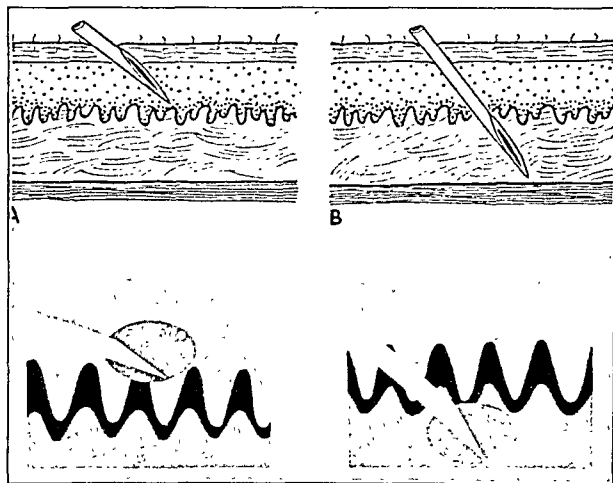


Fig. 1.—Diagrams taken from two recent discussions on the proper site of injection of intradermal inoculations. On the left is indicated the "correct" site and on the right the "wrong" site. The "correct" site is here shown to be in the epidermis.

It was my opinion that no human hand could be so accurate. Though some of the injected fluid might reach the indicated desired site, certainly the majority was injected directly into the corium. This seemed particularly probable since the area of thin skin over the volar surface of the forearm is the site usually chosen.

In order to determine the actual site or at least the usual site of an intradermal injection, the following procedure was carried out: The services of several physicians were enlisted. Each of these men had had considerably more than the usual experience with intradermal tests and inoculations. India ink was placed in a tuberculin syringe fitted with a fine (27 gage) needle. The ink was then injected carefully to produce a typical skin "bleb." This was done in the skin of various animals as well as in human skin of the abdomen and volar forearm. Sections of these typical "blebs" were then taken and put through the usual hematoxylin-eosin stain.

The sections clearly indicated that none of the india ink was injected into the epidermal layer of skin. This was true of all the tissues that were studied. In no instance did the injected ink tend to separate the epidermis from the underlying corium.

From the Indiana University School of Medicine.

All the ink was contained in the corium. The level at which it appeared varied considerably. In some instances that appeared satisfactory clinically, though not giving an ideal "bleb," the india ink actually reached the subcutaneous fat as well as infiltrating the corium.

Typical sections of tests made on the volar surface of the forearm are shown in figures 2 and 3. Here it is seen that



Fig. 2.—Actual section of skin from the volar surface of the forearm following intradermal injection with india ink. Clinically typical "blebs" formed, indicating proper injection. The black mass of the ink is clearly seen to be contained in the upper portions of the corium. In no instance was it found in the epidermis, as indicated in figure 1.



Fig. 3.—Another section similar to the section shown in figure 2.

the injected black ink mass infiltrates the upper layers of the corium without reaching the epidermis. Also indicated is the impossibility of inserting a needle into so thin a layer of epidermis as that present over this site.

23 East Ohio Street.

# METHYL SALICYLATE POISONING

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AND  
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According to the United States Pharmacopeia<sup>1</sup> methyl salicylate (oil of gaultheria, oil of wintergreen, oil of betula or oil of sweet birch) is a colorless, yellowish or reddish liquid having the characteristic odor and taste of gaultheria. It can be made synthetically or by distillation with steam from the leaves of *Gaultheria procumbens* or *Betula lenta*. The law requires that the label show the source of the product but not its toxic qualities. This oil is dispensed freely as a counter-irritant and is also occasionally prescribed in very small doses for internal use. It is the main constituent of some of the "patent medicines" sold for the treatment of rheumatism.

While standard textbooks give only brief mention to methyl salicylate poisoning, nevertheless the symptoms and pathology have been adequately described.<sup>2</sup> Twenty-eight cases of methyl salicylate poisoning due to ingestion were reviewed by Lawson and Kaiser,<sup>3</sup> who added another case in which the medicament was used as a counterirritant.

The clinical and necropsy reports on two recent cases at the Columbus Children's Hospital are presented with the hope that the toxic properties of this drug may be better appreciated and with the suggestion that all bottles containing methyl salicylate be labeled to show its poisonous character.

## REPORT OF CASES

CASE 1.—History.—F. H., a Negro boy aged 3 years, was admitted to the Children's Hospital Feb. 19, 1938, with the complaint of drowsiness for five hours. The past and family history was irrelevant. Eighteen hours previously the patient had taken about 60 cc. of oil of wintergreen, which had been used by a member of the family to massage stiff joints. It was not labeled poisonous nor was it considered dangerous by the family. The child vomited several times immediately after swallowing the drug. He was then given castor oil, which was retained, and was put to bed at the usual hour but did not fall asleep. He became increasingly irritable and restless with a marked increase in the respiratory rate. At 3 a. m. the day of admission the child became very excited, continually throwing his arms about and rolling his eyes. Two hours later he became quiet and would not respond to questions but would become very active if touched. There was no further change in the patient's condition until his admission.

On physical examination the patient was acutely ill and dehydrated; he was well nourished. The rectal temperature was 98 F. on admission. The pulse was 86 per minute and of good quality. Respirations were 50 per minute and very deep. The face was pinched and the eyes were sunken. There was a marked odor of wintergreen on the breath. The pupils were constricted and the ears and nose were normal. There was definite cyanosis of the lips, fingers and toes. The lungs were clear and the heart sounds normal. Neurologic examination gave negative results. The blood count was within the normal range except for a leukocytosis of 20,500 with 77 per cent polymorphonuclears and a marked shift to the left. The carbon dioxide combining power was 19 volumes per cent. The roentgenogram of the chest, as reported by Dr. Huston F. Fulton, showed the heart normal in size and position, and the lung markings essentially negative. The child was immediately given 250 cc. of isotonic sodium lactate intravenously, followed by a continuous intravenous injection of the same material. The stomach was washed with dilute solution of sodium bicarbonate through a nasal tube. The temperature increased to 102 F., accompanied by profuse perspiration. The pulse became more rapid and gradually too weak to count. The respirations remained very deep and rapid. The patient died four hours after admission.

From the Departments of Medicine (Pediatrics) and Pathology of the Ohio State University College of Medicine, and the Children's Hospital.

1. United States Pharmacopeia, ed. 11, Philadelphia, J. B. Lippincott Company, p. 234.

2. Bastedo, W. A.: *Materia Medica, Pharmacology, and Therapeutics*, ed. 4, Philadelphia, W. B. Saunders Company, 1937, p. 475. Dodd, Katherine; Minot, Ann S. and Arena, J. M.: *Salicylate Poisoning*, *Am. J. Dis. Child.* 53: 1435-1446 (June) 1937.

3. Lawson, R. B., and Kaiser, A. D.: *Arch. Pediat.* 54: 509-515 (Sept.) 1937.

**Necropsy.**—External examination of the body showed no pathologic changes. Petechial hemorrhages were found in the visceral pleura of both sides, the endocardium, the pericardium and the epicardial surface of the heart and the gastric and jejunal mucosa. The lungs showed an early bilateral bronchopneumonia with moderate pulmonary edema. This was accompanied by a marked dilatation of the right auricle and ventricle. No odor of methyl salicylate was detected when the intestinal tract was opened; however, the bladder was distended with turbid urine which showed the presence of the drug by the alcohol-ether extraction method. The liver was grossly hyperemic, with evidence of parenchymatous degeneration. In the kidneys there was a similar condition of the tubular epithelium.

**CASE 2.—History.**—V. G., a Negro girl aged 18 months, seen in the outpatient department April 9, 1938, complained of severe coughing of one hour's duration. The baby had been playing with a bottle of oil of wintergreen that had been used for external application. It was not labeled to show its toxic properties. The parents noted that the bottle of methyl salicylate was opened and that the contents were spilled on the child's garments but they were not positive that any had been taken by mouth. A large amount of milk was given to the patient, which was immediately vomited. Physical examination of the child was negative and no odor of wintergreen could be detected on the breath. The stomach was lavaged with dilute solution of sodium bicarbonate. No odor of wintergreen was detected in the gastric contents, which consisted mostly of milk curds. The child seemed normal during the next six hours but vomited all fluids soon after ingestion. She became very restless, remained awake and had a short generalized, tonic convulsion every time she was stimulated. Respirations became rapid and deep.

On physical examination the child was acutely ill, dehydrated and comatose; she was well developed and well nourished. The rectal temperature was 104.6 F. The pulse rate was 160 per minute and of good quality. Respirations were 64 per minute and very deep. The patient was pale, with cyanosis of the fingers, toes and lips, and was covered with a profuse diaphoresis. The fontanels were closed. The eyes were sunken with a fixed, glassy appearance. The pupils reacted to light. No odor of wintergreen could be detected on the breath, but the characteristic "fruity" odor of acidosis was noted. Examination of the chest disclosed rales at both bases; the heart sounds were rapid but otherwise normal. The tendon reflexes were increased in intensity but equal bilaterally. Frequently during the examination short, generalized spasms of the extremities developed. The patient was given 250 cc. of isotonic sodium lactate by hypodermoclysis immediately after admission. The patient soon became comatose and died two hours later, or about twenty hours after taking the drug.

**Necropsy.**—There were no particular marks of a pathologic condition on the body. There was consolidation of the entire lower lobe, the lower half of the middle lobe and the posterior third of the upper lobe of the right lung. The same process was present in all of the lower and most of the upper lobe of the left lung. These areas were a deep red and very firm and contained no air. Severe pulmonary edema was present in the rest of the lungs. Microscopic examination revealed a type of pneumonia characterized by collections of round cells and an early necrosis of alveolar epithelium as found in mustard gas poisoning. This was interpreted as an aspiration type of pneumonia. There was chronic passive congestion and severe parenchymatous degeneration of the tubular epithelium of both kidneys. Passive congestion and parenchymatous degeneration were also present in the liver. Two small superficial erosions of the gastric mucosa were present without hemorrhage. The myocardium was pale with marked dilatation of the right side of the heart. Alcohol-ether extraction of the urine found in the bladder gave a positive test for methyl salicylate.

#### COMMENT

These cases demonstrated the usual clinical manifestations of methyl salicylate poisoning. There were vomiting, rapid and deep respiration, dehydration, profuse diaphoresis, cyanosis, stupor, coma and cardiorespiratory failure. The patients had

severe acidosis which did not respond to treatment. In spite of alkaline parenteral fluids, both of the patients failed to recover. It is felt that alkali as a prophylaxis should be started before symptoms of acidosis develop. It is apparent that oil of wintergreen, sold for use as a counterirritant, should carry a label indicating its poisonous qualities when taken internally.

327 East State Street.

### Special Clinical Article

#### LESIONS OF THE EXTRAHEPATIC BILIARY TRACT

CLINICAL LECTURE AT SAN FRANCISCO SESSION

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In discussing lesions of the biliary tract I should like to direct attention to some of the developments which have occurred in this field in the past year or two. Concerning advances in the surgical treatment of diseases of the biliary tract, I shall discuss, first, cholecystitis; second, errors in the diagnosis of cholelithiasis, and, third, symptoms persisting after operations on the biliary tract.

#### CHOLECYSTITIS

For the past five years there has been a gradual trend toward early operation in cases of acute cholecystitis. This subject was discussed fully at a meeting of the American Surgical Association in 1933, and, although it was generally recognized that each case presents an individual problem, most of those present agreed that as a rule early operation gave the most satisfactory results.

Heuer<sup>1</sup> in 1937 reported a series of 153 cases of acute cholecystitis in which early operation was performed. In 65 per cent of his cases operation was performed on the day of admission of the patient. The loss by death of only five of the 153 patients, a mortality rate of 3.2 per cent, has convinced him that the risk of operation in the acute stage of the disease is not so great as "the danger of gangrene and perforation of the gallbladder, the result of a conservative or waiting policy."

In two and a half years (January 1934 to July 1936) seventy-six patients were operated on at the Mayo Clinic for acute cholecystitis, the diagnosis being confirmed by the surgeon at the time of operation or by the pathologist. There were three deaths, a mortality of 3.9 per cent. In two of the cases in which death occurred the gallbladder had ruptured and localized abscesses had formed. In the third case the gallbladder was gangrenous. In 21 per cent of the cases the gallbladder had ruptured, but in none was general peritonitis found at the time of operation. In about 45 per cent of the cases either the gallbladder had ruptured or rupture was imminent. Cholecystectomy was performed in 80 per cent of the cases, whereas in 20 per cent the amount of inflammation present, both in the gallbladder and in adjacent structures, and the condition of the patient made it seem that cholecystostomy was preferable to cholecystectomy.

From the Division of Surgery, the Mayo Clinic.

Read in the Surgical Division of the General Scientific Meetings at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 14, 1938.

1. Heuer, G. J.: Surgical Aspects of Acute Cholecystitis, *Ann. Surg.* 105:758-764 (May) 1937.

In the decision as to the best management of acute cholecystitis, the following considerations would appear to be of the greatest importance: In almost every case of acute cholecystitis, obstruction of the cystic duct, which is usually the result of impacted gallstones, is present, and unless the obstruction is relieved the obvious pathologic course is perforation of the gallbladder. The perforation may be surrounded by omentum and a localized abscess may develop, or the gallbladder may perforate into an adherent, adjacent viscus, such as the duodenum or colon; some adjacent viscus usually is found intimately attached to the subacutely inflamed gallbladder. Since the attachment of these structures to the gallbladder, and the perforations, are the results of delay in bringing about relief of the obstruction, it would seem obvious that in the early hours in which the acute cholecystitis is present cholecystectomy is the preferable procedure. On the other hand, if the surgeon is not called to see the patient until twenty-four hours or more after the onset of the acute attack, and signs and symptoms of recession of the acute process are manifesting themselves, delay until the inflammatory process has still further subsided is worthy of thoughtful consideration. This applies also in cases in which the patient is not seen until two or three days after the onset of the acute attack, when he is definitely ill not only from the associated processes of infection but from toxemia, dehydration and gastrointestinal stasis. In these cases too observation over a few hours will make it possible to determine whether the patient's condition is improving or not. In the presence of improvement, delay in surgical intervention for a short time usually is advisable.

#### ERRORS IN THE DIAGNOSIS OF CHOLECYSTIC DISEASE

As an introduction to a discussion of the causes of persisting symptoms and their prevention after operations on the biliary tract, I should like briefly to discuss some of the errors in the diagnosis of cholecystitis, cholelithiasis and choledocholithiasis.

As laboratory aids in diagnosis have increased in number and accuracy in the hands of competent men, there has come about an increased tendency to regard the result of roentgenographic examinations, particularly in the presence of gastrointestinal diseases, as the last word in determining the presence or absence of disease in the structures examined. I should not like to give the impression that I am unaware of the tremendous importance of the positive reports of disease obtained by roentgenographic examination. Such reports are practically always accurate and are of great assistance in demonstrating both to the physician and to the patient the presence of disease. On the other hand, nothing will ever take the place of an accurate clinical history or a careful and thorough physical examination. Furthermore, the fact that certain stones in the gallbladder are not opaque to roentgen rays and therefore escape detection is well known. This is particularly true if the stones are not obstructing the cystic duct and if the elasticity of the gallbladder is such that it appears to fill and empty satisfactorily. Emphasizing this point is the frequency with which gallstones are present in so-called normally functioning gallbladders.

It has been my experience that when the result of the roentgenologic examination of the patient who is suspected of having disease of the biliary tract is at variance with the clinical diagnosis, it is of advantage to all concerned to hold discussion with the roentgenologist in order that reexamination may be made. In a

case in which operation recently was performed and in which the patient gave an excellent clinical history of a few attacks of biliary colic, the first roentgenogram of the gallbladder indicated that it was functioning normally. A second roentgenographic examination a few days later revealed the gallbladder to be nonfunctioning, and at operation empyema of the gallbladder was found, together with an ovoid stone which obstructed the cystic duct. It is quite possible that in this case the stone was not opaque to roentgen rays and that it was not obstructing the cystic duct at the first examination. Yet the persistence of the clinician in his clinical diagnosis of cholecystitis led to the demonstration of the pathologic changes by the roentgenologist and enabled the surgeon to proceed with the operation. This case, too, well illustrates the point that, although the roentgenogram gives evidence of disease, it does not give an indication of its extent. On innumerable occasions I have removed an acutely inflamed, edematous gallbladder, the emptying of which was obstructed by stones in the cystic duct, although marked pathologic change was not apparent on roentgenographic examination, in the patient's history or on physical examination. Likewise too much reliance must not be placed on the roentgenologic report of a solitary stone in the gallbladder, for in addition the gallbladder may be filled with smaller stones, some of which may be obstructing the cystic duct and producing associated acute cholecystitis. I have in mind a case in which the roentgenologic evidence of but a single stone in the gallbladder led to postponement for three months of the operation because the patient was 78 years old and her general condition was none too good. When the gallbladder was removed it was filled with small stones, some of which were obstructing the cystic duct.

In the last year or two, largely because of publication of papers dealing with the so-called medical treatment of cholecystitis, there has been an unfortunate tendency to deny operation to patients with cholecystitis who have had few symptoms and to patients who, although they have had symptoms of cholecystitis, have failed to give evidence of stones in the biliary tract on roentgenologic examination. The fallacy of withholding operation from the latter class of patients is apparent in view of the foregoing discussion. To allow a patient who is in good condition except for cholelithiasis to go on to the point of having acute obstruction of the cystic duct or of the common duct, with the resulting complications increasing the risk of a surgical procedure and reducing the completeness of the surgical cure, seems to me unjustifiable.

#### SYMPTOMS PERSISTING AFTER OPERATIONS ON THE BILIARY TRACT

Symptoms which persist after operations on the biliary tract can be attributed directly to one of two causes: 1. There may have been failure to recognize, both before and after operation, that the patient's symptoms were not explained by the condition of the biliary tract. 2. The presence of lesions in the biliary tract other than those in the gallbladder may not have been recognized; such lesions are stones in the common or cystic ducts, cholangitis, pancreatitis, carcinoma of the bile ducts, of the ampulla or of the pancreas, and abnormal functioning of the sphincter of Oddi.

It must be remembered that other lesions may produce symptoms which mimic those of disease of the biliary tract, and the presence of these lesions must be excluded whenever possible in examination of the patient prior to operation and by exploration of the sus-

pected structures at the time of operation on the biliary tract. Among these lesions are perforating ulcers of the posterior duodenal wall, calcareous disease of the urinary tract and hydronephrosis. To this list can be added the less frequently occurring referred pain of angina pectoris, gastric crisis of tabes and the pseudo-cholecystitis of neurasthenic women.

Although space does not permit elaboration on all these important lesions or on the differential diagnosis between these lesions and those of the gallbladder, I must refer to most of them because of their great importance in evaluation of the cause of symptoms which persist after cholecystectomy.

*Cholelithiasis.*—I have been much impressed with the great number of cases in which I have found stones in the common bile ducts in the course of an operation on the gallbladder but in which the presence of these stones had not been suspected prior to operation. The stones had not been discovered before operation largely because the patient had not given any evidences of biliary obstruction, such as jaundice or the intermittent hepatic fever of Charcot. Such experiences led to investigation by Trueman and me of the percentage of cases in which stones of the common duct occurred without producing evidence of biliary obstruction. In 35 per cent of 200 consecutive cases in which stones had been removed from the common bile duct in the course of an operation recently performed at the Mayo Clinic it was found that there had not been evidence of jaundice at any time, and in 63 per cent fever had not been present.

Obviously, if stones in the common, hepatic or cystic ducts are overlooked, symptoms will persist. Only occasionally will stones be expelled from the common duct into the duodenum, because the sphincter of Oddi tends to hold them within the duct. In reply to a question as to how to prevent the overlooking of stones in the common duct, one can reply that all stones will increase the diameter of the common bile duct. Hence the finding of an enlarged common bile duct is indication for exploring its interior. Exploration can be done with the finger if the size of the duct permits; otherwise a set of graduated scoops can be used. In most instances the smaller stones will be picked up in the hollow of a scoop, and, after the bulbous ends of these instruments have been gently forced through the sphincter of Oddi, small stones within the intrahepatic ducts, which may have escaped detection by any means, are afforded an opportunity, during the patient's convalescence, of finding their way into the duodenum.

The frequency with which stones in the common duct are associated with disease of the gallbladder is further apparent in a series of 812 cases<sup>2</sup> in which operation was performed at the Mayo Clinic in 1936 for benign lesions of the gallbladder and bile ducts. In 182 of these cases the ducts were opened and explored because of their large size, and in 109 stones were found in the common or hepatic ducts. In the remaining seventy-three cases the enlargement of the ducts was the result of pancreatitis, spasm or inflammation of the sphincter of Oddi and the patient received benefit from the drainage of the common duct.

*Stones in the Cystic Duct.*—Not infrequently in the performance of cholecystectomy an elongated cystic duct is allowed to remain, and this may also contain an unsuspected stone. I have operated in five such cases

in the past two years, and in all of them, at the secondary operation, not only was the stone in the cystic duct of good size but the cystic duct had enlarged and its wall had become subacutely inflamed. In one case the attacks of pain were so severe that the patient had become a morphine addict. After removal of the stone from the cystic duct and removal of the dilated inflamed stump of the cystic duct, it was possible to rid the patient of his pain and of his morphinism within two weeks.

*Cholangitis and Pancreatitis.*—It will be recalled that stones were found in 109 of the 182 cases in which the common bile duct was explored because of its enlargement, whereas in the remaining seventy-three cases stones were not found in the common or the hepatic bile duct. Evidences of cholangitis with associated pancreatitis in these seventy-three cases were turbidity of the bile, the finding of gram-negative bacilli of the colon group, with or without staphylococci or streptococci, and thickening of the head of the pancreas, as determined by palpation. Further confirmation of this diagnosis was obtained in the postoperative choledochograms, which in some cases revealed persisting stasis in the biliary tract, apparently due to edema of the pancreas, evidenced by demonstrable narrowing of the pancreatic portion of the common bile duct.

The development of the cholangitis and pancreatitis, in my opinion, was secondary to the cholecystitis. Failure to recognize associated inflammatory lesions of the liver and of the pancreas and failure to drain the common bile duct are the causes in some cases of symptoms persisting after cholecystectomy. In many such cases, in which a secondary operation has been performed on the common bile duct after cholecystectomy and stones have not been found, infected bile and thickening in the head of the pancreas have been demonstrable. Removal of the inflamed gallbladder, exclusion of the presence of stones in the common duct by exploration of the duct with scoops and by choledochograms and drainage of the common bile duct with a T tube for a sufficient time to allow cholangitis and pancreatitis to subside have relieved the symptoms and cured the patient.

*Carcinoma of the Bile Ducts and the Head of the Pancreas.*—Carcinoma of the bile ducts usually occurs at the junction of the cystic and the common duct or at the bifurcation of the hepatic ducts. In the early stages the tumor usually is small and somewhat circumscribed and it is difficult to distinguish the condition from edema of the duct secondary to stone without cutting through the tissues concerned. Such exploration offers the opportunity to take a specimen for biopsy, which will confirm the diagnosis. When, however, the ductal tumor is at the ampulla, it may be so small that its presence is not recognized by palpation. If this is the case, if the gallbladder is diseased and if stones are present, the biliary obstruction may seem to be the result of one of the benign lesions previously described, for instance stone of the common duct or associated cholangitis, or pancreatitis. Remaining obstruction of the common duct, however, manifests itself clinically by persistence of a biliary fistula after the drainage tube has been removed from the common duct. The presence of obstruction would have been revealed had a choledochogram been made before removal of the T tube, for the choledochogram would have given evidence of the obstruction persisting at the lower end of the common duct.

2. Walters, Waltman, and Gray, H. K.: Annual Report for 1936 of Surgery of the Stomach, Duodenum and Biliary Tract, Proc. Staff Meet., Mayo Clin. 12: 561-565 (Sept. 8) 1937.



Stone in the gallbladder and in the common bile duct is not an infrequent accompaniment of malignant tumor of the ducts and of the ampulla. Nevertheless, I never have seen stones in the gallbladder associated with carcinoma in the head of the pancreas unless the carcinoma in the head of the pancreas was due to extension of a cancer originating in the pancreatic portion of the common bile duct.

*Abdominal Function of the Sphincter of Oddi.*—That an abnormally functioning sphincter of Oddi, with or without associated spasm of the first portion of the duodenum, will produce biliary colic as a result of increased intrabiliary pressure was demonstrated clinically and experimentally by Butsch and McGowan<sup>3</sup> while they were fellows in the Mayo Foundation. These investigators also found that reduction of intrabiliary pressure, with relief of pain, could be temporarily obtained by administration of glyceryl trinitrate or by inhalation of amyl nitrite. Their results have great clinical value, for these antispasmodic substances have relieved patients who were having attacks of pain subsequent to an operation on the biliary tract whereas, contrary to expectation, morphine in average doses instead of relieving the pain increased it as a result of increasing the intraductal pressure.

When a patient who has postoperative biliary colic obtains relief from his pain by administration of glyceryl trinitrate and amyl nitrite, the clinical impression is likely to become fixed that the cause of the pain is primarily spasm of the sphincter of Oddi or of the duodenum. This impression may be erroneous, for the spasm may be secondary to the presence of stone in the common duct. This I have found to be the case in several cases in which I have operated. I should like to emphasize, therefore, that the only way to exclude the possibility of that most frequent cause of biliary colic subsequent to cholecystectomy, namely stone of the common duct, is by exploration of the interior of the duct. If the surgeon fails to find stones in the common duct it is advisable to dilate the sphincter of Oddi. This, as has been said, not only will allow but may assist overlooked small stones within the intrahepatic ducts to pass more readily into the duodenum. To dilate the sphincter of Oddi the graduated, rounded scoops used to explore the common duct for stones are used, for not only do they serve to engage smaller stones in their hollow but their rounded, bulbous ends serve as excellent dilators of the sphincter. This method has been used at the Mayo Clinic for many years as a routine in every case in which the common bile duct was opened and explored. If the scoop did not pass into the duodenum it could be assumed that the obstruction at the lower end of the common bile duct had not been completely removed, and this has led to removal of impacted stones in the ampulla which might otherwise have been overlooked. How long dilatation of the sphincter of Oddi lasts when obtained in this fashion is under investigation at present.

*Duodenal Ulcer Producing Symptoms Simulating Disease of the Biliary Tract.*—It is noteworthy that patients who have lesions of the biliary tract may have symptoms which suggest duodenal ulcer. Such symptoms are more frequent in males than in females and

occur most often when complications of the lesions of the biliary tract, such as cholecystoduodenal fistula, have occurred. Interestingly enough, there are certain duodenal ulcers, particularly those on the posterior wall of the duodenum, which perforate into the pancreas and produce crisis-like attacks of pain simulating biliary colic. This may lead to the clinical diagnosis of a lesion of the biliary tract, especially if jaundice and edema of the head of the pancreas, resulting from perforation of the ulcer, are present. Roentgenoscopic and roentgenographic examination of the stomach and duodenum and of the biliary tract are of the greatest assistance in distinguishing between these two lesions. In some cases in which there are duodenal ulcers of the posterior wall there is not enough disturbance of motility of the anterior wall of the duodenum to indicate their presence on roentgenoscopic and roentgenographic examination. It should be a routine in operations on the biliary tract therefore to examine the stomach and duodenum. In the examination of the duodenum an ulcer of the posterior wall is likely to be overlooked, in the absence of scarring on the anterior wall, unless the posterior wall is palpated between the thumb and the forefinger; if it is palpated thus, the crater of the ulcer can be detected. I have operated in several cases of this type in which cholecystectomy had been performed previously without relief of symptoms and in which the presence of a stone in the common duct was suspected. Roentgenographic examination of the stomach and duodenum failed to reveal an ulcer, but at operation an ulcer of the posterior duodenal wall was found on palpation and its presence was demonstrated by opening the duodenum. After the duodenum had been opened the common bile duct was explored, and it was determined that it did not contain stones.

*Angina Pectoris.*—In the discussion of differential diagnosis of disease of the biliary tract, the warning always is given that in an attack of angina pectoris pain which simulates that of disease of the gallbladder may be referred to the epigastrium and that, under these conditions, if the biliary tract is operated on the patient is likely not to survive the operation. In my opinion there has been gross exaggeration of the risk of operative procedures in cases of angina pectoris and even in cases in which coronary thrombosis previously has occurred. In addition the fact has been overlooked that a badly diseased gallbladder may produce pain referred to the substernal and precordial regions; this pain may lead to the erroneous diagnosis of angina pectoris and the patient may be denied operation. In such cases roentgenographic examinations of the gallbladder, if they have given positive evidence of disease, have been of great value. It has been shown by Fitz-Hugh<sup>4</sup> and others that in cases of angina pectoris removal of the diseased gallbladder has had a marked beneficial effect on the patient's cardiac condition. Fitz-Hugh has been able to prove this effect by the improvement in the appearance of the electrocardiographic tracing subsequent to operation. Moreover, pain of the type of angina pectoris which appears or recurs after operation on the biliary tract may be attributable to one of the persisting conditions of the biliary system which have been discussed in the foregoing paragraphs.

3. Butsch, W. L., and McGowan, J. M.: Pressure in the Common Bile Duct: Preliminary Report, Proc. Staff Meet., Mayo Clin. 11: 145-150 (March 4) 1936. McGowan, J. M.; Butsch, W. L., and Walters, Waltman: Pressure in the Common Bile Duct of Man: Its Relation to Pain Following Cholecystectomy, J. A. M. A. 106: 2227-2230 (June 27) 1936.

4. Fitz-Hugh, Thomas, Jr., and Wolfert, C. C.: Cardiac Improvement Following Gallbladder Surgery: Electrocardiographic Evidence in Cases with Associated Myocardial Disease, Ann. Surg. 101: 478-483 (Jan.) 1935.

ADVANCES IN THE SURGICAL TREATMENT OF  
LESIONS OF THE BILIARY TRACT

Patients who have stones in the gallbladder and who postpone their removal are only awaiting obstruction of the cystic duct, with consequent acute cholecystitis, or expulsion of the stones into the common bile duct, with biliary obstruction. In addition the irritative effect of stones in the gallbladder is the most frequent cause of malignant changes therein; carcinoma of the gallbladder practically never occurs without the presence of stones. These facts would seem to be impressive evidence of the necessity of surgical removal of such lesions even though the gallstones seem to be producing few symptoms.

When one considers the present approach to perfection of surgical treatment, its relative safety in the hands of well trained surgeons and the efficiency of anesthesia, the mortality rate of cholecystectomy for patients who are in good condition should not exceed 1.5 per cent. Should stones obstruct the cystic duct and acute inflammation develop, the minimal mortality rate reported for surgical treatment for acute cholecystitis varies from 3 to 4 per cent,<sup>5</sup> and this mortality rate increases proportionately, depending on the experience of the surgeon and the condition of the patient. When stones in the common bile duct produce obstructive jaundice, the operative mortality rate is increased to a minimum of 3.5 per cent, and it may increase to 10 per cent or more, depending on the patient's general condition and the experience of the surgeon. There does not seem to me to be any stronger argument for surgical treatment of cholecystitis and cholelithiasis before such complications have had a chance to occur.

*Indications for Surgical Treatment.*—It would seem to me therefore that the indications for surgical treatment of lesions of the biliary tract are as follows:

Surgical exploration should be undertaken if the patient presents clinical evidence of disturbances of the biliary tract. This applies particularly to those patients who have biliary colic and to those whose symptoms are characteristic of the so-called qualitative food dyspepsia of cholecystitis. If roentgenographic evidence confirms the clinical diagnosis of disease of the biliary tract, surgical exploration is even more definitely indicated. Should the patient's clinical history be typical of disease of the biliary tract and roentgenographic examination be negative, exploration is warranted. If roentgenographic examination gives evidence of the presence of stones, surgical exploration should be made regardless of the size and number of the stones that the roentgenogram seems to show. The possibility of error in this respect has been commented on in detail early in the paper.

If the patient has previously undergone an operation on the biliary tract and still has pain resembling that of biliary colic, or if he has jaundice or pain associated with pylorospasm, exploration of the common duct is indicated. Whether previous operation has been performed or not, if jaundice is present and if intrahepatic jaundice can be excluded, and perhaps even when it cannot be excluded, and there are a few such cases, exploration should be made. The reason for this declaration is that, just as there is no other way to exclude the possibility that the biliary tract is the site of obstruc-

tion if jaundice is absent, so is it difficult to determine before exploration the exact cause of the obstruction if jaundice is present. The possibility of a stone's remaining in the stump of the cystic duct distal to the point where it is divided in the operation of cholecystectomy necessitates careful palpation of the cystic duct or search of its interior with a scoop. The enlarged common bile duct should always be opened and explored with scoops even if stones cannot be palpated along its course.

*Immediate and Postoperative Cholelithography.*—Mirizzi<sup>6</sup> and Hicken, Best and Hunt<sup>7</sup> have called attention to the value of making a cholelithogram at the time of operation. The method consists in injecting into the common duct at operation a substance that is opaque to roentgen rays. In most cases in which stones are present this medium is displaced and the displacement can be demonstrated by roentgenograms at the time of operation. Although I have not been impressed with the necessity of this procedure, believing that exploration of the duct with scoops is adequate, postoperative cholelithograms I believe to be of great importance, and in the last three years I have used them as a routine in my service in all cases in which T tubes have been inserted into the common duct in the course of an operation on the biliary tract. This method has enabled undiscovered stones to be detected. In one case in my service it was possible to cause fragmentation of the stone by introduction of ether into the duct, and passage of the fragments into the duodenum was facilitated by administering amyl nitrite, thus bringing about relaxation of the sphincter of Oddi.<sup>8b</sup> In another case persisting stasis in the common duct, the result of a swollen pancreas, was demonstrable by cholelithograms for several weeks after operation. In two cases this method made it possible to demonstrate that the cause of the obstruction was a malignant rather than an inflammatory tumor of the ampulla of Vater.

Since by cholelithograms overlooked stones in the common bile duct can be detected, an effort should be made to assist their passage into the duodenum by causing their fragmentation with ether, as previously referred to, and by dilation of the sphincter of Oddi with such substances as amyl nitrite and glyceryl trinitrate before operative removal is undertaken. Similar benefit is offered by administration of dehydrochloric acid and relaxation of the sphincter of Oddi by instillation of warm solutions of oil into the duodenum, as suggested by Best.<sup>8</sup>

*Blood Transfusion and Vitamin K.*—In preoperative and postoperative treatment of patients who have complications of lesions of the biliary tract, I have become more than ever impressed with the value of giving transfusions of blood to jaundiced patients. As a method of reducing the incidence of hemorrhage and of improving the efficiency of parenchymatous organs of the body it is without an equal. A close second, however, is intravenous injection of dextrose.

Recently Snell and his collaborators<sup>9</sup> of the Mayo Clinic have corroborated Quick, Stanley-Brown and

5. (a) Walters, Waltman, in discussion on Wesson, H. R., and Montgomery, T. R.: Acute Cholecystitis: Report of Eighty-Seven Cases, Proc. Staff Meet., Mayo Clin. 12: 500-503 (Aug. 11) 1937. (b) Walters, Waltman, and Wesson, H. R.: Fragmentation and Expulsion of a Common Duct Stone into the Duodenum by Using Ether and Amyl Nitrite, Surg., Gynec. & Obst. 65: 695-697 (Nov.) 1937. (c) Heuer.<sup>1</sup>

6. Mirizzi, P. L.: La cholécystectomie sans drainage (cholécystectomie idéale), Paris, Masson & Cie, 1933.

7. Hicken, N. F.; Best, R. R., and Hunt, H. B.: Cholangiography: Visualization of the Gallbladder and the Bile Ducts During and After Operation, Ann. Surg. 103: 210-229 (Feb.) 1936.

8. Best, R. R.: Cholangiographic Demonstration of the Remaining Common Duct Stone and Its Nonoperative Management, Tr. West. S. A., to be published. Best, R. R., and Hicken, N. F.: Biliary Dysynnergia: Physiological Obstruction of the Common Bile Duct, Surg., Gynec. & Obst. 61: 721-734 (Dec.) 1935.

9. Butt, H. R.; Snell, A. M., and Osterberg, A. E.: The Use of Vitamin K and Bile in Treatment of the Hemorrhagic Diathesis in Cases of Jaundice, Proc. Staff Meet., Mayo Clin. 13: 74-77 (Feb. 2) 1938.

Bancroft's<sup>10</sup> observations that the blood of jaundiced patients is deficient in prothrombin and that this is responsible for the hemorrhage. They have increased the prothrombin of the blood by administration of vitamin K, bile and bile salts. The preparation of vitamin K, which they used, was made from putrefied fish meal. Smith, Warner and Brinkhous<sup>11</sup> have obtained similar results with use of an extract of alfalfa.

#### SUMMARY

There is an increasing tendency for surgeons to recognize the value of early operation in cases of acute cholecystitis. In some instances the advocates of delayed operation, I believe, have in mind cases not of acute but of subacute cholecystitis, in which more than twenty-four hours has elapsed since the onset of the acute attack. When the attack is in the acute stage the patient's temperature and pulse rate are elevated. If the acute inflammatory process is retrogressing and the patient's general condition improving, delay may be advisable.

The most frequent cause of error in the diagnosis of lesions of the biliary tract has been failure to recognize the importance and the significance of the clinical history. Especially is this the case if roentgenologic examination fails to demonstrate the presence of disease. Attention is directed to the fact that many gallstones are not opaque to roentgen rays and fail to be visualized in cholecystograms. Therefore the roentgenologic report regarding the number of stones visualized and their position may not agree with the number and position of the stones that actually are present. Likewise the roentgenologic report of a nonfunctioning gallbladder is not always an indication of the degree of pathologic change present.

Symptoms which persist after operations on the biliary tract usually are the result of overlooked lesions of the common and hepatic ducts, infections of the liver and pancreas and malignant tumors of these structures, including the ducts. Patients who harbor extrinsic lesions, such as perforating ulcers of the posterior duodenal wall and renal calculi, may give histories suggesting disease of the biliary tract. The possibility that any or all of these lesions coexist with disease of the gallbladder must be investigated as accurately as possible both prior to and at the time of operation, for if they are overlooked persisting symptoms are inevitable. Particular attention is directed to the large number of cases in which unsuspected stones are present in the common bile duct and in which jaundice never has been present, stones being found only by exploration of the interior of the enlarged duct. In the absence of stones of the common duct other causes of pain are pancreatitis and spasm of the sphincter of Oddi and of the duodenum.

The indications for surgical treatment of lesions of the biliary tract can be defined as follows: Surgical exploration should be undertaken if the patient presents clinical evidence of disturbances of the biliary tract. This applies particularly to patients who have biliary colic. With such patients, when other possible causes of the symptoms have been excluded, exploration of the gallbladder and ducts should be carried out even though roentgenograms fail to give evidence of disease.

Postoperative roentgenologic studies of the common bile ducts following introduction of an opaque substance into them (choledochograms or cholangiograms) have proved of definite value in determining causes of persisting obstruction in the common duct such as overlooked stones, pancreatitis and carcinoma of the ampulla and of the pancreas.

The value of the new substance vitamin K in increasing the amount of prothrombin in the blood and decreasing the tendency to bleed is a noteworthy advance in the preoperative and postoperative treatment of patients who have obstructive jaundice.

## Special Article

### CONFERENCES ON THERAPY

#### II. TREATMENT OF CORONARY DISEASE

NOTE.—These are actual reports, slightly edited, of conferences by the members of the Departments of Pharmacology and of Medicine of Cornell University Medical College and the New York Hospital. The questions and discussions involve participation by members of the college staff, students and visitors. The next report will concern "Disorders of Cardiac Rhythm."—Ed.

DR. LEWIS A. CONNER: The topic for consideration is coronary thrombosis and angina pectoris, or better perhaps the angina of effort. In both instances coronary artery disease is implied in the title.

While it is very simple indeed to distinguish between a typical case of angina of effort and a typical case of coronary thrombosis—the symptoms of these I mean—there are many cases in which these distinctions which we shall emphasize this morning fall away and one is in great doubt as to whether one is dealing with a straight case of angina of effort, which implies that there is no permanent structural change, or whether we are dealing with a closure of some very small arterial branch. As one becomes more and more familiar with the clinical picture of these coronary cases one recognizes that these intermediate cases which are hard to identify are comparatively common.

Moreover, we have to bear in mind that many of the cases of coronary closure which go on even to infarction of a certain area of the cardiac muscle are not cases actually of coronary thrombosis. We may have occlusion of the branch of an artery by gradual arterial sclerotic thickening until the artery or the branch is actually occluded, without there being necessarily present any thrombosis. Commonly, of course, we see the two things together: there is a certain amount of arterial sclerotic change and then in that badly diseased artery or branch we get finally an actual acute thrombotic closure; but sometimes without any thrombus formation the gradual closure of the artery by the arteriosclerotic process may finally reach a point at which infarction occurs, which will give rise to symptoms not distinguishable from those of an acute coronary thrombosis.

I will take up first angina pectoris or, as it seems to me much better to name it, the angina of effort. You are all familiar with the clinical picture. You know that it represents a sudden development, a momentary development, of some change in the heart which produces this typical cardiac pain, typical in its location, typical usually in its radiation, varying greatly in severity, but with this characteristic feature that the

10. Quick, A. J.; Stanley-Brown, Margaret, and Bancroft, F. W.: A Study of the Coagulation Defect in Hemophilia and in Jaundice, *Am. J. M. Sc.* 190: 501-511 (Oct.) 1935.

11. Smith, H. P., Warner, E. D., and Brinkhous, K. M.: Prothrombin Deficiency and the Bleeding Tendency in Liver Injury (Chloroform Intoxication), *J. Exper. Med.* 66: 801-811 (Dec.) 1937.

pain and distress are only momentary, that they pass off within a very few seconds or a minute or two, that they are produced almost always by some form of effort, most commonly physical effort of course, but often enough by excitement or some violent emotional reaction. From the fact that after the attack is over the patient seems none the worse for it—he may have such attacks for years without any other serious heart symptoms—we have to conclude that, whatever is happening, there is not a permanent structural change in the course of this momentary group of symptoms. The familiar, usual explanation is that there has been for a moment a sudden contraction, or spasm we call it, of the coronary arteries or some portion of the coronary arteries, and a momentary ischemia of the heart muscle; but it must be only a spasmodic functional contraction because in a few moments the symptoms are all over and the patient is just as well as he was before.

Are there other symptoms than those of the pain with its characteristic radiation? Is dyspnea a feature of an attack of angina of effort? Indeed, it is striking in its absence as a rule. A man who is walking along the street, walking up a grade, doing some heavy work or who perhaps gets into a quarrel and gets tremendously excited has this attack of pain with its typical radiation. He usually stands still because of the pain, but after he has had a few attacks he stands still because he knows that the moment he stops his effort, the moment he stops these unusual demands on his heart, the pain will pass off. Usually, dyspnea is not an accompanying feature at all.

Is faintness a symptom?

ANSWER: No.

DR. CONNER: No.

How about palpitation?

ANSWER: No.

DR. CONNER: Are there any other symptoms?

(There was no response.)

DR. CONNER: Are there any other symptoms usually than those that we have described, than the characteristic pain? As a rule, there are not; nothing but the pain. That pain is relieved very soon on the cessation of the special effort, whether physical or emotional, which caused the heart to work harder.

I think we ought to dwell on the matter of the pain a little longer, particularly its characteristics and perhaps its cause. Dr. Gold, are we to look to you for an explanation of its cause?

DR. HARRY GOLD: I prefer not.

DR. CONNER: Why does this pain arise? Well, we have suggested that it arises because of the abnormal change in the heart muscle, some momentary ischemia, probably due to a spasm of some one or other of the coronary arteries or of some of their branches. I do not know that anybody knows exactly what happens or why the pain comes. Are the experimentalists in a position to say that the pain is directly the result of a coronary spasm, Dr. Gold?

DR. GOLD: No, I think there is a good deal of doubt as to how it comes about, and there are various views.

DR. CONNER: I think so. For our own comfort it is well to have this theory of spasm in mind as a possible explanation, but I think it is far from proved. That might be taken up in a discussion of some of the drugs and their effects I should think.

The question of the duration of the pain is an interesting one. A man will be walking along briskly

and will be able to walk a certain distance. In the same individual the distance is often quite uniformly the same; I mean if he walks at a certain pace he knows from experience that he can walk between one and two blocks, let us say, and then the pain comes on or begins to come on, and unless he stops and rests it will become severe. If he insists on going on it will become perhaps so intense that he has to stop. But suppose he goes the block and a half and feels the pain coming on and stops, how long does it last then?

Well, in the early stages when the symptoms are brought on chiefly by these physical efforts the relief is usually very prompt—within, oh, a few seconds or a half minute or a minute or a minute and a half after the patient has stopped or begun to rest, the pain is pretty well gone. Sometimes you will be told that it takes actually between five and ten minutes, but I do not think that that is usually the case and I am not sure that such statements are always reliable. When you have a very severe pain, one minute or two seems a long time. But in this individual, as time goes on, the attacks become more frequent and perhaps begin to come with excitement and even merely after a substantial meal without effort or without excitement, and then the promptness with which they are relieved either by treatment or by rest diminishes, and the pain may last five, ten, fifteen minutes or half an hour, if the attack is a severe one, before there is complete relief. However, in typical cases the pain is usually relieved within a minute or two at most on cessation of the effort, and even sooner if medicine is taken.

As far as the radiation of the pain is concerned, you know, I think, how varied the radiations are. One of the most characteristic things is for the pain to be centered in the midline, not over the apex of the heart or well to the left over the heart, but really behind the sternum. Sometimes it is low down, sometimes it is high up, often it is described as a pain that is not localized so sharply at the sternum but across the chest. And then together with that there is the radiation of the pain usually down the left arm, often down the inner side of the arm sometimes to the ulnar distribution in the fingers, sometimes to the back of the shoulder, sometimes to the back, very often indeed up along the side of the neck to the jaw or temple. As I said, in the great majority of cases the radiation is perhaps altogether to the left, but there are cases in which the radiation is altogether to the right, and there are many more cases in which it may be chiefly to the left but still is noticed to the right. There are cases in which if the pain is not very severe there is no radiation and the radiation comes only with a very severe attack; on the other hand there are cases in which the first pain is felt not behind the sternum but in the arm, and then as the severity increases the pain travels in the reverse direction from the arm to the chest. There are innumerable variations that occur and it is necessary to understand them.

I think we might take up now the question of the treatment of these attacks, confining the discussion for the time being to the attacks of the angina of effort; that is, attacks of angina pectoris and not attacks in which there is actual closure, mechanical closure, structural closure, of the artery. I have spoken of rest as the method of treatment which the patient himself invariably uses and which in many cases is entirely effective. The pain stops so promptly after stopping the effort that the use of a drug is not called

for at all, but there are many other cases in which drugs are required, and I shall ask Dr. Gold to speak of them.

[Before Dr. Gold spoke he listed the following drugs: (1) morphine, (2) nitrites, (3) xanthines, (4) barbiturates, (5) digitalis, (6) quinidine, (7) epinephrine.]

DR. GOLD: As regards the use of drugs in the treatment of coronary artery disease, I might say first of all that there are no drugs that affect the disease directly and that the treatment of coronary disease by means of drugs resolves itself into the treatment of a number of symptoms or perhaps symptom groups. There is one exception to that. Any one interested in the exception might ask a question about it when we are finished.

The symptoms are pain, restlessness, anxiety and fear. These are all important symptoms that arise at one time or another in the course of coronary disease.

Heart failure, congestive heart failure, is a functional disorder which sometimes occurs in the course of coronary artery disease. Shock is a matter that often needs to be treated in the course of coronary artery disease at one stage. This, again, shows that what we are treating in coronary artery disease are certain functional disorders but not the disease itself.

I want to make a few remarks about the common drugs that are used in the course of coronary artery disease. First of all, there is morphine. The place of morphine in coronary artery disease is only for the relief of pain in the course of coronary thrombosis. How much morphine is a question that is worth while considering. I have here a paper that was written only four years ago on the treatment of coronary thrombosis, and one statement in this paper is as follows: "During the acute attack, relief of pain can only be accomplished, and even then too slowly, by giving a half grain of morphine hypodermically and repeating as necessary. Other substitutes for this drug are worthless, and smaller doses do no good." Half a grain of morphine, and repeat as necessary; other substitutes are worthless!

I wonder about that advice. There is no doubt that there are a great many cases of coronary thrombosis in which the pain is so very severe that only large doses of morphine are necessary, but on the whole I have a feeling that we use morphine much more freely in coronary thrombosis than is necessary.

As Dr. Conner indicated, there are a great many cases of coronary thrombosis in which the course of the pain is almost indistinguishable from the course of the pain of an attack of effort angina, and in those cases of thrombosis the pain is often not very severe and, what is more important, does not last very long, so the administration of half a grain of morphine and the repetition of that dose is unnecessary and is likely to result in poisoning.

Briefly, what are the dangers of using morphine in coronary disease? What are some of the things that should lead us to think twice before administering such large doses as these?

First of all, we know that morphine causes vomiting in a fairly high proportion of cases and, since in coronary thrombosis we aim to maintain the patient as free of muscular effort as possible, such violent muscular movements as are involved in vomiting can prove disastrous. Vomiting after morphine is also fairly persistent. Sometimes it lasts as long as six or eight hours in repeated attacks. That helps to complicate the picture in coronary thrombosis because occasionally

the disease itself causes vomiting and it is often difficult to distinguish whether the patient is vomiting as the result of the treatment or of the thrombosis. I have known of instances—a very striking one I saw not so long ago—in which repeated doses of morphine were given to control the vomiting which was caused in the first instance by the morphine. Morphine not only stimulates the vomiting center but it also depresses it. In animals morphine exerts an antiemetic action, but in man usually this action is not marked. Often in an individual in whom a dose of morphine has caused vomiting a repetition of the dose will continue to cause vomiting. The depression of the vomiting mechanism is rare in man. That is one point.

The other point which I think is important to stress is the fact that morphine vomiting is very persistent and may last from six to eight hours. Remember that, particularly in cases in which there is some doubt as to whether or not the continued vomiting is due to the coronary thrombosis.

Morphine also causes spasm of sphincters, particularly the sphincter of the bladder, and urinary retention may well be produced by large doses of morphine. Many of the cases of coronary thrombosis occur in men at the age of 55 or 60 who have difficulty as a result of a chronic prostatic enlargement and our giving large doses of morphine often increases that difficulty.

A further point is this: In view of the fact that so many cases of coronary thrombosis occur in older people, large doses of morphine should be used with great caution because old people are likely to be more sensitive to the respiratory depressant action of morphine than young ones.

Another point grows out of a remark that Dr. Conner made and is extremely important from the standpoint of the use of morphine, and that is the short duration of the pain in some attacks of coronary thrombosis. The pain may not last several hours; sometimes it is over within fifteen or twenty minutes. If that pain is very severe and you give half a grain of morphine and then repeat the dose within a half hour or so, that patient has then received a whole grain of morphine. A grain of morphine in a normal man within a short period of time will sometimes produce considerable respiratory depression, more particularly, as I said before, in elderly people. In a patient with coronary thrombosis this respiratory depression is not likely to be seen so long as the pain is there, because pain, as I believe we mentioned last time, is an antidote to morphine; but just as soon as the pain ceases spontaneously, what occurs is what you are likely not to be expecting unless you bear it in mind, namely profound respiratory depression. Those are some of the dangers of using very large doses of morphine.

From time to time one encounters a patient who is receiving a quarter of a grain of morphine two or three times a day, and the only reason why he is receiving the morphine is that he has had a coronary thrombosis rather than that he is having very severe pain. Pain, and severe pain, is the indication for the use of morphine in coronary thrombosis, and in that case we should also bear in mind that the less morphine that we can manage with, the better.

I do not mean to indicate that we ought to withhold morphine and allow the patient to suffer very severe pain, but to bear in mind that there are dangers in large doses of morphine, and that as little as will suffice to control the pain should be used.

Are there any substitutes for morphine? This question is raised by the article I quoted: "Other substitutes for this drug are worthless, and smaller doses do no good."

Again, I believe that what the author has in mind is the case of coronary thrombosis which perhaps at the present time is not the most common variety, the case in which the pain is very severe and lasts many hours. In the more common variety the pain is over in a short time and is not nearly so severe, and these patients often get along perfectly well with codeine. In these cases a grain of codeine phosphate or half a grain given subcutaneously will often serve as satisfactorily as morphine, without the dangers of respiratory depression which applies to morphine.

A curious fact about morphine is that in animals morphine is much less toxic than codeine. In the dog, for example, 50 or 60 mg. of codeine per kilogram will cause death; 250 mg. of morphine is necessary to cause death. But the reverse is true in man. In man codeine is a much safer drug than morphine. From 2 to 3 grains of morphine will often paralyze the respiration in a normal man, but from 2 to 3 grains of codeine produce little effect on the respiration in man.

It is perhaps worth while saying a word about how morphine relieves the pain. Morphine does not relax directly the smooth muscle of the coronary arteries. Morphine causes spasm of smooth muscle, also spasm of the smooth muscle of the coronary vessels. Furthermore, morphine is a parasympathetic stimulant, as we know from the actions of morphine on the pupil and as we know from the actions of morphine on the heart rate. The parasympathetic presumably carries the major vasoconstrictor control of the coronary vessels; we should therefore expect morphine really to increase the spasm of coronary vessels. The chief action of morphine in relieving pain is central, and it is due to the blocking of the perception of pain at the centers, without any direct beneficial effect on the vessels or their nerve supply.

There is another popular substitute for morphine that I might speak of, and that is pantopon. Probably some of you may have heard of some one's using pantopon in this hospital. It is widely used, and it is said, of course, that pantopon has many advantages over morphine. Without going into details, I want to make the statement that pantopon has no advantages over morphine. It is in effect nothing but a diluted morphine. A half grain of pantopon contains about a quarter of a grain of morphine, and the action that one obtains from a half grain of pantopon is similar to that of a quarter of a grain of morphine. All sorts of situations will arise from time to time that will lead you to think this may not be so. You may give a patient a quarter of a grain of morphine and the patient may vomit, and if you still require additional relief from the pain you may turn to pantopon and give a dose of pantopon, and the patient may not vomit. That is the kind of observation that leads to the statement found in the advertising circulars that pantopon is not as actively emetic as morphine. Please remember that the same results can be obtained with morphine. A patient will sometimes vomit after one dose of morphine and not vomit a few hours later when given a second dose. In animal experiments we can show that in a striking manner. In giving a series of daily doses of morphine we find, for example, that the first dose caused vomiting, the second did not, the third did, the fourth did, and the fifth did not, and so on. It has

an extremely variable kind of effect, and one should not be deceived by the occasional observation which seems to indicate that pantopon produces any effects other than those of its content of morphine.

A rather interesting comparison of pantopon and morphine in pain appeared in an article in a recent issue of *THE JOURNAL*, in which the authors were unable to distinguish in the slightest between the actions of morphine and pantopon when pantopon was given in similar amounts so far as the morphine content was concerned.

Now as to the nitrites. The nitrites are presumed to relieve pain of effort angina by relaxing smooth muscle. The relaxation of smooth muscle accomplishes two purposes: One to relax the coronary vessels themselves to increase the coronary flow, and the other to relax the systemic blood vessels so as to lower the systemic blood pressure. The latter reduces the load on the heart, thus introducing a second factor by which the pain of effort angina is relieved. That explanation is true only if we assume, what is now being more or less generally assumed, that effort angina is due to a relative cardiac ischemia, that the amount of work demanded of the heart is out of proportion to its circulation, whether that occurs as the result of a primary spasm of the vessels with no extra work, or whether it occurs without a spasm of the vessels but with an extra load being thrown on the heart. That then is the explanation, provided our previous assumption regarding the mechanism of pain is true. We are not altogether certain that it is the true explanation of effort angina.

There is a danger, of course, in lowering the systemic pressure too much because, while lowering the pressure decreases the load on the heart it also diminishes coronary flow, and we can defeat the purpose by giving too much of the nitrites—glyceryl trinitrate or any of the nitrites.

A patient will often ask whether there is any danger in the continued use of the nitrites. The answer to that is there seems to be none at all, and patients who have effort angina should receive as much of the nitrites as appears to be necessary to keep them as free as possible from attacks of pain.

Again referring to a statement that Dr. Conner made about the character of these attacks of effort angina: They are very likely to come to an end as soon as the patient ceases effort or as soon as an excitement is over. In cases of that kind the nitrites have but little value. All that the nitrite can do is to give the patient a headache, because before the nitrite has had an opportunity to exert its effects the pain is over if the patient only stops. Therefore it is perhaps true that in a considerable proportion of patients with angina of effort the nitrites have no place at all.

The question of the prevention of these attacks by the nitrites I think has not received as much attention as we might well give it. There are patients who have very brief attacks of pain but a great many of them during the day, ten, fifteen or twenty attacks of pain, and an attack of pain seems to be precipitated by almost anything they do. These people are in a very bad way; they have pain when they lie in bed and there is very little that one can do for them. From time to time you may spare these patients a good deal of suffering by the administration of nitrites for the prevention of attacks,  $\frac{1}{150}$  grain of glyceryl trinitrate administered under the tongue every hour or every two hours. That



seems like a lot of things to be doing during the day, but these patients are very glad to do anything because they suffer so much, and here and there a patient having fifteen or twenty attacks of pain a day, if subjected to nitrites in the routine fashion of  $\frac{1}{150}$  grain every hour or two as the case may be, will have the number of attacks of pain very considerably reduced.

Again, will any habit result from the continued use of nitrites? The answer to that is also no. Apparently the doses of the nitrites that are generally used in the treatment of angina pectoris in the manner described do not establish habit. In the course of the treatment of a patient with effort angina, the patient may report to you that he has had an attack of pain which has not responded to the nitrite. This appears like the development of tolerance but one should raise the question as to whether the patient has not developed an attack of coronary thrombosis. An electrocardiogram at that point will often help to establish a diagnosis. I am quite certain that there are many cases of coronary thrombosis that are overlooked because the attacks resemble fairly closely the previous attacks of effort angina, with this one exception that it fails now to respond to the nitrites.

There are many things that can be discussed about the treatment of these conditions, but perhaps we might interrupt the direct discussion to allow time for questions that you may have about either morphine, the nitrites or any of the other compounds that I have listed on the black board.

QUESTION: What dose of morphine do you suggest as proper?

DR. GOLD: In the treatment of an attack of coronary thrombosis?

QUESTION: Yes.

DR. GOLD: I wonder whether Dr. Conner would care to answer that.

DR. CONNER: I think what has just been said is true, but I should hate to have the emphasis left on the dangers of morphine in coronary thrombosis. There are dangers and, of course, to say as that article did that the thing to do is to give a half grain and repeat that as often as necessary, and that anything less than that is a waste of time, is an exaggeration and almost an untruth; but the fact of the matter is that there are a great many cases of coronary thrombosis in which the emergency is so supreme, where the agony is so terrific, that quarters of morphine are not felt at all, and in those one has to give large doses of morphine, more indeed than you like to give often, in order to get anything like relief from the horrible agony. It is much safer I think to give a quarter at intervals of ten minutes, if necessary, rather than to give a half. I do not think I ever gave a half at one time, but certainly within an hour you may have to have as much as a grain. On the other hand, as Dr. Gold has said, there are many cases in which the pain is not very severe, the duration is not very long and it would be folly to start off with a half grain of morphine.

I have a feeling myself—perhaps it is not justified—that the morphine does a good deal more than merely make life tolerable so far as the relief of pain is concerned. It seems to me that it covers up in some way the horrible fear, the morbid feeling that these people have that their last moment has come, that they are in the grip of some perfectly overwhelming catastrophe. I think that one sees the collapse relieved and the cold

sweat and the tremendous peripheral failure that is present relieved to some extent by the morphine. I think it does something more than merely relieve pain, and in my experience it is the only drug that seems to have any effect in the severe cases of coronary thrombosis with their overwhelming group of symptoms.

I am interested in what Dr. Gold said about codeine. My own experience has been that, while codeine is often very helpful, when you have to give fairly large doses you get a series of complications. You get a lot of headache. You get dulness and heaviness. You get constipation. Therefore it seems to me there are a number of objectionable side effects of codeine, so that I often feel that a sixth of a grain of morphine will frequently do more good in the relief of pain than will a grain of codeine. That is a matter of individual choice, but the point is that in coronary thrombosis—I mean where the pain is very severe, with the collapse and all present—morphine is the only thing that really, as far as I know, has any effect.

Are you going to speak about digitalis, Dr. Gold?

DR. GOLD: I think there are some people here who are charged up with questions concerning digitalis therapy.

DR. JOHN E. DEITRICK: I should like to ask Dr. Gold what his feeling is about giving digitalis when there is definite evidence that the patient has had a coronary occlusion and is beginning to show mild signs of heart failure. Would he digitalize that patient?

DR. GOLD: I have no hesitation at all about digitalizing the patient who has had a coronary thrombosis and is showing signs of heart failure.

DR. DEITRICK: How would you give the digitalis?

DR. GOLD: I should give it more or less as I would to the ordinary patient who was showing signs of heart failure. I would take two or three days to digitalize the patient fully if the symptoms were not too rapidly progressing, or take twenty-four hours to do it if the symptoms were fairly rapidly progressing, and I should use on the average a dose of about a gram to a gram and a half of a good powdered leaf.

DR. CONNER: Would you do that in the early stage of a coronary thrombosis, Dr. Gold, if you had signs of heart failure?

DR. GOLD: If there were definite signs of failure I would have no hesitation in digitalizing a patient even within thirty-six hours after the onset. That is, in the case of heart failure and not peripheral circulatory failure; I really mean rales in the lungs and an enlarging liver, marked dyspnea and that sort of thing which one so seldom sees in a patient with acute coronary thrombosis.

DR. DEITRICK: Would you feel safer in giving digitalis to a patient only thirty-six hours after the onset of sudden pain than in giving it ten days after the occlusion?

DR. GOLD: From experimental observations I should feel safer in giving it within ten hours than ten days, but the only difference would be in the size of the dose. I should be more cautious about the dose if I were digitalizing the patient ten days after an acute coronary thrombosis than within the first twenty-four or thirty-six hours. That view is based entirely on experimental results. Animals are more susceptible to digitalis ten days after coronary occlusion than they are within the first twenty-four hours afterward.

DR. DEITRICK: Isn't it true that if human beings do not die within the first two or three days the next most dangerous period would be around two weeks afterward, when they may die suddenly?

DR. GOLD: But I would say that that would not influence the question of digitalization at all.

DR. DEITRICK: You mean that if the patient is showing signs of failure, so that it is obvious he will die of heart failure, it is worth taking a chance of perhaps getting a sudden reaction, or exitus even, but give digitalis anyhow, for the number you can help.

DR. GOLD: I think the danger of giving digitalis in coronary thrombosis with heart failure is overrated. I doubt very much whether any serious consequences would follow. One of the dangers that it is believed will follow came up only a short time ago here in the hospital. Wasn't it here that a patient with coronary thrombosis was digitalized and died soon afterward as the result of a ruptured ventricle? I do not think digitalis had the slightest thing to do with the development of the rupture. First of all a ruptured ventricle occurs (it is not very common, but it occurs) in people who have never been digitalized and, what is more, in man digitalis does not raise the systemic blood pressure. It does so in the dog, and it raises the intraventricular pressure in the dog, but it does not do so in man. According to all present indications it increases the efficiency of the heart muscle but does not really increase the intraventricular pressure directly.

In cases in which the heart is failing sufficiently to require digitalis, I should say it would be a mistake to withhold it.

DR. DEITRICK: One reason why I brought that up is that I think that a number of the students here have seen us digitalize patients rapidly and fully within twelve to sixteen hours. Do I understand that you would not like to digitalize so rapidly in patients with coronary thrombosis unless they were going into an acute pulmonary edema?

DR. GOLD: I think that point is important because the patient with coronary thrombosis may be more susceptible to digitalis so that less digitalis is necessary to produce the usual effects. We found in animal experiments that, three weeks after a coronary occlusion, animals require only about three fourths of the dose of digitalis that in the normal animal will cause death or will cause ventricular tachycardia. Beyond that there are no hazards that one can see experimentally, so that it would be wiser to proceed more slowly in order not to encounter the danger of overrunning in regard to the dose.

DR. CONNER: You are speaking now of the early periods. According to your experimental work, you would give the digitalis within a day or two after the infarct has developed.

DR. GOLD: There are two kinds of experiments: one in which we tie off the coronary vessel, and within the first twenty-four hours we administer digitalis and determine how much is necessary to cause a ventricular tachycardia and how much is necessary to cause death. Within the first twenty-four hours this animal requires exactly the same dose as a normal animal without coronary thrombosis. Then we have another series in which the injection of digitalis is made three weeks after the acute closure when there is a partially healed infarct, and at that time the animal requires only three

fourths of the dose of digitalis necessary for the normal animal to cause both the ventricular tachycardia and the fatal effect.

DR. CONNER: May I say a few words on the subject of digitalis?

DR. GOLD: You certainly may.

DR. CONNER: I speak only from the clinical aspect, but I think among clinicians the opinion is almost always, in fact almost universally, held that digitalis is dangerous. Because an opinion is almost universally held does not necessarily mean it is a correct opinion, but it has been developed by long, continued clinical experience. I have a dread of digitalis in the early periods of coronary thrombosis. Now that may be unjustified. I am not prepared to say whether it is or not, but I cannot believe that if we have a grave attack of coronary thrombosis, with the closure, let us say, of the left descending branch, of a large infarct, a freshly established infarct, that we are likely to help the patient's chances of life by attempting to whip up the remaining heart muscle to supernormal action. Of course the first and obvious thing to do is to keep the patient absolutely quiet, to demand as little of the heart as possible. When you have done that, and when you have quieted the patient and overcome shock and pain by morphine, I think you have done everything you can do safely, and I have urged for years the avoidance of digitalis at that period of the cardiac infarction. I do not think the danger of rupture is the thing that is to be feared in giving digitalis, but we do know that when death occurs in the earlier stages of coronary thrombosis the common cause of death is the development of abnormal rhythm with ultimate ventricular fibrillation. Isn't that your idea, Dr. Gold?

DR. GOLD: Yes.

DR. CONNER: It seems to me that at least digitalis might increase this tendency toward the development of ventricular fibrillation. Whether it will or will not or whether it does or does not I do not know but I would prefer to take my chance with an early infarct and signs of failure without the use of digitalis but with merely the absolute rest and morphine as necessary. I may be quite wrong, but I have that feeling very strongly.

DR. DEITRICK: Would you use a diuretic, such as mercupurin, if the patient began to have rales, respiratory difficulty and diminished urinary output and the blood pressure had dropped 50 points, although not enough to cause shock? Would you use a diuretic to improve the fluid output?

DR. GOLD: I should feel that would be a safe procedure.

DR. DEITRICK: I should like to ask Dr. Gold about that because I think it depends entirely on the pharmacology. If mercupurin or a similar drug causes hydremia of the circulating blood and an increase in blood volume, it would cause an increased load on the heart; but if it acts only on the kidney and does not affect the circulating blood volume or lower the specific gravity of the blood, then it ought to be indicated in this case. Otherwise in the patient developing pulmonary edema it would only tend to increase the pulmonary edema. Is that statement correct?

DR. GOLD: I think I follow your statement.

First of all, the diuretics rarely cause any appreciable hydremia. There are some experiments indi-

cating that there is some dilution of the blood after one of the mercurial diuretics, but I think that there are just as many which fail to show it. I think that the problem of increasing the load by the diuretic is not important. I should say that the diuretic action occurs in some other way and that other way does not contraindicate its use in the heart failure in the course of coronary thrombosis.

Might I say also that from the practical standpoint the difference between Dr. Conner's view and our view concerning digitalis is not nearly as great as it seems because the number of cases of congestive heart failure in the first few days of a coronary thrombosis are very few, aren't they?

DR. CONNER: Yes.

DR. GOLD: They are so few that we are rarely confronted with that problem, and when one hears about using large doses of digitalis in the early days of a coronary thrombosis, one finds the person referring to the kind of individual who shows peripheral failure, circulatory failure, shock, rather than congestive heart failure in which the liver is descending and the lungs are filling up and there is marked dyspnea. The latter kind of picture in which digitalis might prove useful is quite rare in the acute stages of coronary thrombosis.

## Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING ARTICLE.

HOWARD A. CARTER, Secretary.

### ELECTROLYSIS

A DISCUSSION OF EQUIPMENT, METHOD OF OPERATION, INDICATIONS, CONTRAINDICATIONS, AND WARNINGS CONCERNING ITS USE

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NEW YORK

This article is prepared especially for those who are not familiar with the technic of application of electrolysis, the equipment and its uses.

Electrolysis is far from being a safe procedure in unskilled hands. Carelessness and ignorance when applied to electrolysis may cause injuries to the skin which are objectionable, disfiguring, painful and even, at times, dangerous.

Electrolysis, incorrectly termed "surgical ionization," involves the destruction or decomposition of tissues with the negative pole of a galvanic current. In chemistry the term electrolysis designates the decomposition of a chemical compound—that is, the separation of an electrolyte in solution into its constituent parts by a galvanic or direct current. Electrophoresis, incorrectly termed "medical ionization," includes iontophoresis. When medicaments are applied to the body either the positive or the negative pole may be the active electrode, depending on the drug used. The remaining indifferent electrode is used on some other portion of the body. Electrophoresis may be utilized without the necessity of employing any drugs. MacKee<sup>1</sup> states that it is averred that with the negative pole there is vaso-

dilatation and a softening effect on new formed tissue (scars), while with the positive pole there is vasoconstriction and hardening.

Electrolysis is very useful for the treatment of certain conditions. In fact it is the only method for permanent and safe removal of unwanted hairs on various parts of the body. It is also the method of choice in treating many other dermatologic conditions. Michel<sup>2</sup> in 1875 successfully cured a case of trichiasis by the use of electrolysis.

#### APPARATUS

Any apparatus used for medical purposes has both advantages and disadvantages. It is well before using any new instrument to be especially familiar with the dangers. The apparatus employed by most American dermatologists consists of a 22½ volt dry battery hooked up to a small rheostat, a milliammeter and two binding posts, plainly marked positive and negative. More elaborate apparatus has an off and on switch and also automatic reels for the cords. Cords leading from the binding posts are flexible and are made up of insulated fine copper strands. The active electrode is connected to the negative pole and consists of a needle holder and needle. The dispersive or inactive electrode is connected to the positive pole, in turn connected to a sponge. The battery, rheostat, milliammeter, switch, binding posts and reels may be neatly mounted in a small box measuring approximately 12 inches in width, 10 inches in depth and 6 inches in height (fig. 1). The wiring diagram of a typical electrolysis unit is given in figure 2.

The needle holder should be light in weight, should be small and should grip the needle firmly. Some needle holders form a straight line with the needle. Others form a little more than a right angle to the needle. The latter holder is used by most dermatologists. A spring contact on the holder for making and breaking the current is a little bit cumbersome and awkward to operate. Either an insulated needle or a fine blunt pointed steel needle may be used for the removal of hairs. The insulation on a needle reaches within 1 mm. of the end, serving to concentrate the current at this point. Some dermatologists use platinum needles, but for the most part a steel needle is employed. Insulated needles have the advantage of causing less pain when a greater current is used. The point may be dull or sharp and is preferably rounded. The smallest and lightest needle obtainable is generally employed.

The dispersive or inactive electrode consists of a handle, insulated by wood and attached to a sponge which is held in the patient's palm. Some physicians prefer to have the patient dip the hand in a saline solution, which is contained in a metal basin, in turn attached to the positive binding post of the apparatus. The milliamperage ordinarily employed varies between 0.25 and 1. For special conditions up to 2 milliamperes may be used. The milliamperage is controlled by a small rheostat and may be read on the milliammeter (fig. 1).

When using electrolysis for epilation, forceps which are light and flexible and which have a smooth grasping surface and tapering blunt points are preferred (fig. 3).

Every operator must be familiar with the method of testing his apparatus for polarity. This is done by attaching the needle to what is believed to be the negative pole. The sponge is attached to the positive pole.

1. MacKee, G. M.: Handbook of Physical Therapy, Chicago, American Medical Association, 1937, p. 386.

2. Michel, Charles E.: St. Louis Clin. Rec. 2: 145, 1875.

Then the two are inserted into a vessel containing water or physiologic solution of sodium chloride. Should small bubbles form around the needle (negative electrode) and rise to the surface of the water, correct polarity is indicated. If the needle and sponge were reversed, this bubbling would not be noticed. A faster method for determining polarity of a portable galvanic machine employs red litmus paper. When moistened with distilled water, this will turn blue if touched with the negative pole of a direct current. It will not change color when in contact with the positive pole of a direct current. In performing this test, one must complete the circuit by drawing both electrodes across the paper. The importance of correct polarity must be emphasized, because if a steel needle were attached to the positive pole and inserted into the skin or follicular opening there would be a deposition of iron with the resultant formation of a permanent iron tattoo mark, manifested as tiny black dots.

#### TECHNIC

The patient may lie on a flat table of a height convenient for the operator. Sometimes a special chair is used somewhat similar in type to that used by barber shops. The operator sits on a swivel stool in back of the patient, providing a resting place for his arms and hands. Artificial light is of the same intensity at all times and is therefore preferred to daylight. The light should be adequately and properly shaded and easily adjusted. Magnification is not essential but one having poor eyes will find the Beebe binocular loupe helpful in treating small superficial lesions and fine hairs. The technic varies with the lesion treated.

For the removal of hair<sup>3</sup> the following method is employed by most dermatologists: The patient and the operator get in proper position, with the light adjusted (fig. 4). The area to be treated is first washed with soap and water, and cleansed with benzine or carbon tetrachloride to remove all fatty substances. It is then dried with sterile gauze, and 70 per cent alcohol by weight is applied. The operator's hands are thoroughly scrubbed with soap and water and rinsed with alcohol. The needle is sterilized by immersion for ten minutes in alcohol and is attached to the negative terminal. The needle holder must be clean and a surgically clean towel is put over the patient's eyes in order to protect them from the light and also for the deposition of removed hairs. The patient holds a wet sponge attached to the positive terminal in the palm of her hand. The operator is now ready to insert the needle into the follicle. That portion of the hair projecting above the surface of the skin is used as a guide for the needle. By delicate manipulation, the direction and the depth of the follicle are easily and quickly found. While the needle is held in place with the right hand, approximately 0.5 milli-ampere of current is allowed to act on the hair follicle. As a rule not more than one minute of time nor more than one milliamperage of current is essential for this operation. Every few seconds the hair which is being treated is grasped by the forceps, which is held in the left hand, and a slight tug is given to the hair. If the hair has been thoroughly acted on by the galvanic current it will slide out of the follicle easily. The needle is then withdrawn. This process is repeated on the next hair. Contiguous hairs should not be removed, because

the current is apt to set up a mild inflammatory condition of the skin preventing healing. As a rule not more than three or four hairs are removed from a dime sized (18 mm. in diameter) area of skin. Dimpling of the skin, resistance to the entrance of the needle, edema, delayed appearance of the foam on the surface, excessive pain and muscular contraction indicate improper insertion of the needle. Experience and development of a fine sense of touch will tell the operator when he has reached the bottom of the follicle. No rule can be set down because the length of different follicles varies. The usual length of each treatment is approximately thirty minutes and the interval between treatments is approximately one week.

After the treatment the skin is swabbed with alcohol and dried, and calamine lotion with 1 per cent phenol is applied. Occasionally it is necessary to prescribe a

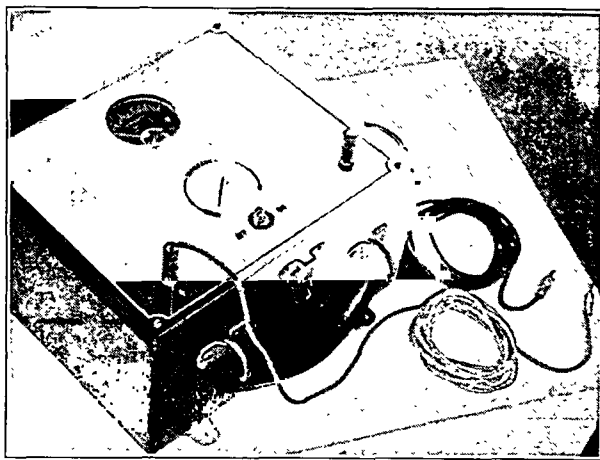


Fig. 1.—Electrolysis unit showing milliammeter, rheostat control, on-off switch and binding posts plainly marked for positive and negative (home-made equipment).

mild lotio alba to be used at bedtime in order to prevent the formation of pustules. In order to obtain good cosmetic results the operator should observe the following rules:

1. Hairs should not be removed from inflamed areas.
2. A test treatment should be given to ascertain the toleration of the skin of various parts of the body.
3. One should always use the smallest amount of current that will effectively and permanently remove hair. A mild current usually suffices for the upper lip.
4. Contiguous hairs should not be removed at one sitting.
5. The needle should not be left in the follicle longer than is absolutely necessary.
6. The needle must pass through the orifice of the follicle and it must be in or very close to the hair bulb.
7. The parts to be treated should be cleansed first with soap and water, then with a fat solvent and finally swabbed with alcohol. After the treatment, an antiseptic shake lotion should be used for from twenty-four to forty-eight hours.

The proper control and manipulation of a single needle require the utmost muscular coordination, good eyesight, many months of experience and much patience. The difficulties encountered in controlling one needle are obvious. One can easily understand how much more difficult it would be to try to insert properly into the follicles and to control at the same time from eight to twelve needles. It therefore appears that the advantages claimed for the multiple needle method of electrolysis cannot be substantiated. What usually happens is

3. MacKee, George M., and Cipollaro, Anthony C.: Principles and Practice of Physical Therapy, Hagerstown, Md., W. F. Prior Company, vol. 1, chapter 18, p. 61.

that the needles are inserted into the skin and not into the follicles. It is very doubtful that more hairs are removed in a given time by the multiple needle method than by the single needle method.

Anesthesia is not required. Various skin anesthetics are ineffectual. The discomfort after the first few treatments is really slight. Most patients soon get used to the treatments. The removal of hair by electrolysis can

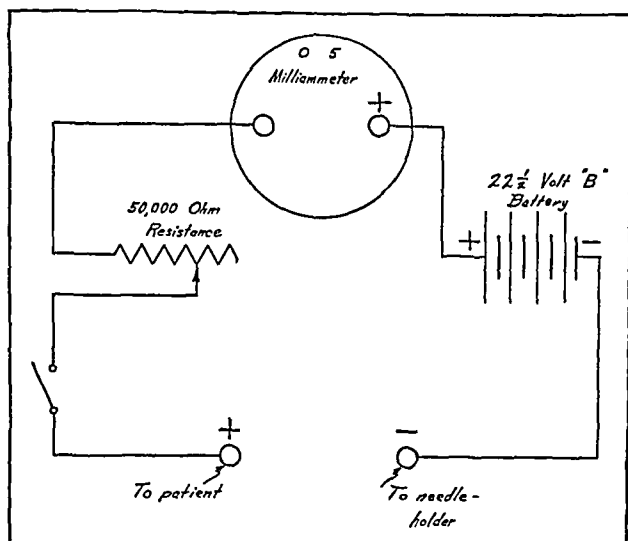


Fig. 2.—Wiring diagram of electrolysis unit.

be mastered by most students. Some, however, are unsuited for this work because of temperament, poor eyesight, tremor or other physical defects. The work is exceedingly tedious, is very difficult and is a strain both physically and mentally.

The ordinary small pigmented hairy mole may be best removed by electrolysis. The hair is first removed as described. Then what remains of the nevus is treated by crisscross (transfixation) insertions of a sharp pointed, uninsulated, fine steel needle. At first the needle, held parallel to the skin, is inserted through the center of the lesion. Several insertions parallel to the first are made and, when the lesion is entirely covered, insertions are made at right angles to the first. During the entire procedure the needle is charged. For larger lesions 1 milliamperes of current is used and for smaller ones from 0.5 to 0.75 milliamperes is sufficient. The lesion is not completely destroyed at one sitting. Several sittings at weekly or bimonthly intervals are necessary. The average mole requires from three to four treatments. Successive treatments are not given until after the reaction from the previous treatment subsides. The treatment of nevi should not be entrusted to lay operators because they lack the requisite knowledge to differentiate benign moles from those which may be actuated into malignant neoplasms by trauma. Even a physician who is well trained, undertaking the treatment of moles with electrolysis, should satisfy himself of the nature of the lesion.

The technic for the treatment of dilated capillaries differs from that used in hypertrichosis and nevi. Dilated capillaries occur in rosacea, in nevus araneus, following overexposure to radium or x-rays, and in other conditions. These telangiectatic vessels are quickly cured by electrolysis. The needle is inserted vertically in several places along the course of the vessel. For small capillaries, single insertions are sufficient. When

treating a spider nevus, the needle is inserted vertically in the center of the lesion and is allowed to stay in place for about a minute. At the end of this time the area appears slightly edematous and blanched, having the appearance of a wheal following an insect bite. When treating telangiectasis by electrolysis, following overexposure to radium or x-rays, one must be extremely careful as to how the treatment is applied. Energetic treatment may break down the radiodermatitic tissues, resulting in ulcer formations. Since the vessels are quite superficial, the needle need not be inserted deeply.

The small common wart and venereal, flat, filiform and digitate warts can be permanently and completely destroyed by inserting the needle vertically into the center of the lesion or by the crisscross (transfixation) method as described under the treatment of nevi.

Senile and seborrheic keratoses that have not undergone epitheliomatous transformation are occasionally treated by electrolysis. The method employed is the same as that for verrucae. Benign new growths such as adenoma sebaceum, multiple benign cystic epithelioma, tricho-epithelioma, syringocystadenoma and hydrocystoma are often cured by treatment with electrolysis. Slightly raised lesions that are small may be treated by vertical insertions, whereas the larger lesions are treated by transfixation of the needle.

It is advisable to discuss at this point the many serious conditions that result from improperly performed electrolysis. This procedure is widely used by laymen, most of whom are unqualified because of lack

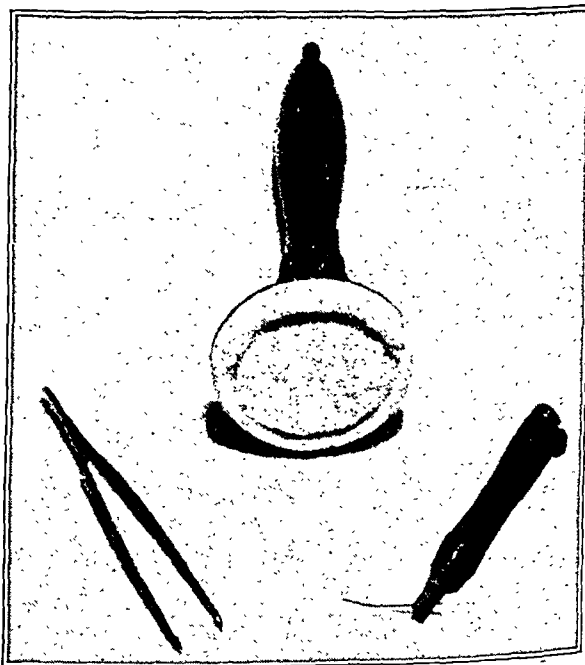


Fig. 3.—Sponge, needle-holder with needle in position, and forceps.

of experience and training. They work under such misleading names as electrologists, hair specialists, dermatologists and beauty culturists. Some lay operators become very proficient in the mechanical handling of the needle but they lack the necessary training that would enable them to differentiate benign from malignant lesions, to avoid infection, to institute proper antisepsis and to prevent disfiguring scars. A lay operator

taught by a physician and working under the supervision of a physician and qualified by training and experience is invaluable. Electrolysis involves not only the actual manipulation of the needle holder as is taught by many commercial houses but also a fundamental knowledge of many phases of medicine, including anatomy and bacteriology. This knowledge is possessed only by physicians.

#### SCARS AND PITS

The permanent disfigurements of scars and pits probably result more frequently than any of the other complications. Those possessing inadequate knowledge or who are not experienced and poorly trained generally apply too much current or leave the current on too long. More often in treating hypertrichosis the electrically charged needle is not in the follicle and several insertions through the skin produce scars and pits. This permanent damage of the skin frequently affects the patient psychologically. Some persons become intropective and may even develop a mild inferiority complex. The return of the hair adds considerably to the mental agony of these patients and may cause them to become psychopathic.

#### INFECTION

A complication that also occurs frequently is infection. As a rule only a small pustule develops where the needle was inserted. This may result from improper sterilization of the needle, inadequate sterilization of the integument, improper cleansing of the hands of the operator or lowering of the resistance of the skin by the combined trauma of the electric current and the insertion of the needle. Occasionally more profound infections may occur, even to the point of causing abscess formation. It is even possible for erysipelas to develop around one of these infected areas. When the infection occurs in the nose, on the upper lip and over the glabella it may be so serious as to cause death, since there is a direct venous communication between these areas and the lateral sinuses. Expert medical operators will never traumatize the tissues within the nose and will not remove hairs from the glabella, eyebrows and upper lip without careful preliminary practical sterilization of the hands, affected areas and their instruments.

#### EDEMA, BLOOD AND PAIN

The improper insertion of the needle may cause an edematous reaction around the needle. When this occurs while one is treating hypertrichosis the needle should be withdrawn because it is not in the hair follicle. A small droplet of blood appearing around the needle indicates that a small blood vessel has been punctured. In some cases ecchymotic areas and pigmentation occur. Pain is more severe in highly sensitized persons than in others. It is also more marked when electrolysis is performed on a patient who has had insufficient sleep or is fatigued from other causes. Excessive pain is experienced when too much current is used or when the needle pierces the skin or goes through the hair follicle. In certain idiosyncratic individuals tiny depigmented areas around the follicular openings may occur and in others even tiny keloids may develop. It is therefore important that some time elapse between the first and the second treatment, so that the physician may have an opportunity of observing the results of the first treatment. It is also essential that the first treatment be a short one so that the patient will gradually become accustomed to the operation.

#### MISTAKEN DIAGNOSIS

Many dermatologists have had brought to their attention patients with malignant neoplasms who were treated for something else by electrolysis. There should be no difference of opinion among physicians as to the undesirability of lay operators without medical supervision using methods that may not only fail to cure the condition but actually lead to serious sequelae. Frequently basal cell epitheliomas may have the general appearance of a fibroma, a nonpigmented nevus or even a pigmented nevus. Only a dermatologist is capable of diagnosing these conditions, and sometimes the differential diagnosis is so difficult that it is necessary to remove tissue for a microscopic examination. It is necessary to state here that electrolysis is not the proper method of treating pigmented and nonpigmented basal cell epitheliomas. Even more serious than this, there are some pigmented lesions which are called benign melanomas. As long as these lesions are not traumatized they remain benign, but as soon as they are treated by such inadequate methods as electrolysis they become malignant and metastases may occur in remote areas of

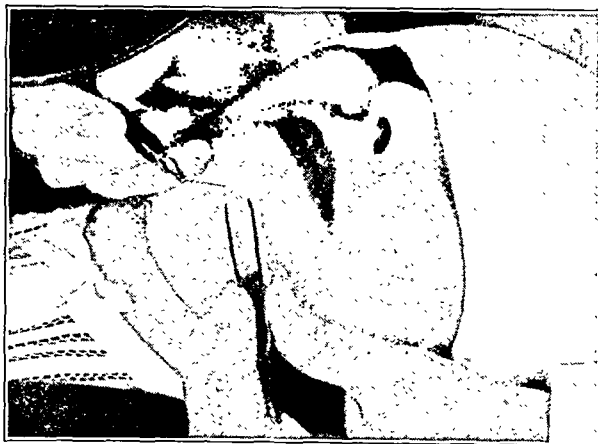


Fig. 4.—Patient lying on table and operator sitting behind patient in proper position for treatment.

the body within a short time. Angiosarcomas have similarly been mistaken for benign moles with the same serious consequences. Lewis<sup>4</sup> mentions a case in which a syphilitic gumma was treated several times by means of electrolysis.

#### CONCLUSION

It should be pointed out that electrolysis is a valuable agent for the treatment of many conditions. It is the only agent that will safely and adequately cure hypertrichosis. Carelessness, inexperience and ignorance have caused undesirable injuries to the skin and other serious consequences. The operator must have at least an elementary knowledge of the anatomy of the skin, of bacteriology, of antisepsis, of tissue tolerance to trauma, of the chemical reaction involved in electrolysis, of the physics and mechanics of the apparatus used. He must know especially how to differentiate benign lesions amenable to electrolytic treatment from potentially dangerous lesions which they simulate. It is obvious that this modality can be properly used only by physicians qualified by training and experience or under their direct supervision.

40 East Sixty-First Street.

4. Lewis, George M.: *Electrolysis in Skin Disorders*, M. J. & Rec. 134: 234 (Sept. 2), 272 (Sept. 16) 1931.



# THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, DECEMBER 31, 1938

## THE GRAND JURY INDICTS

Elsewhere in this issue appears the complete text of the indictment of the American Medical Association et al. by the special grand jury in the District of Columbia. An indictment is not a conviction! Apparently the grand jury which examined only witnesses called by the attorneys of the Department of Justice and such documents as were subpoenaed from the headquarters office believed with Mr. Thurman Arnold that such an indictment would be one way of clarifying the law, which it seems the Department of Justice finds confusing. Space is not available in this index number to recapitulate for our readers the chronologic history of this case; the complete record will be made available in an early issue. Physicians should remember in the meantime that every action of the Association has had the approval of the House of Delegates; that every step has been in the interest of advancing medical science and the quality of medical service for all the people; that the House of Delegates has already authorized the Board of Trustees to fight this case to the courts of last resort to determine the issue.

## SURGICAL TREATMENT OF ESSENTIAL HYPERTENSION

The possibility of influencing chronic arterial hypertension by surgical intervention necessarily involves the study of mechanisms which in a precise and sensitive manner control and regulate the circulation. Variations in arterial pressure are influenced by the cardiac activity, its rate, the output, the circulating blood flow and the peripheral resistance or the vasomotor tone. These factors were believed to be under the direct central automatic regulation. The validity of this concept, however, was considerably impaired by the experiments of Pagano and Siciliano, who in 1900 demonstrated the existence of the carotid sinus mechanism by which the carotid blood pressure controls reflexly the general arterial pressure. By means of a special group of nerve fibers originating in the adventitia of the arteries of the carotid bifurcation, mainly in the carotid bulb and

in the endothelial lining of the vessels of the carotid ganglion, this region is connected with the central nervous system.

Heymans<sup>1</sup> demonstrated in dogs that the general arterial blood pressure is automatically controlled by means of the endovascular pressure itself, acting on the pressosensitive nerve endings of the carotid sinus. So sensitive is this regulation that an increase or a decrease of 1 mm. of mercury pressure from the normal arterial pressure is sufficient to produce reflex compensatory changes. The endovascular pressure itself, according to Heymans, regulates automatically the cardiac output, the circulatory blood volume and the peripheral vascular resistance so well that the arterial pressure is maintained within normal limits or quickly restored to them. This "homeostasis of the arterial pressure" is affected mainly by the intermediation of the pressoreceptor innervation of different arterial and venous areas. It was further shown that vascular reaction to the carotid sinus pressoreceptor reflexes takes place mostly in the splanchnic area; that is, in the mesenteric vessels, the spleen, the liver and the kidneys.

The arterial blood pressure further regulates the secretion and discharge of epinephrine, thus adding the factor of hormonal control. Heymans, however, points out that the adrenal regulation is only an accessory regulating mechanism, since the reflex neurovascular regulation of the blood pressure occurs quite well in the absence of adrenal medullary secretions. In addition to pressoreceptors the carotid gland possesses chemoreceptive nerve fibers which react to changes in oxygen or carbon dioxide content in the blood. Thus far it has been established that the proprioceptive regulation of the general vascular tonus is effected through reflexes the pressoreceptors of which are situated only in certain well localized vascular areas, namely the carotid sinus and the cardio-aortic, veno-auricular, pulmonary arterial and thoracicosplanchnic zones.

In addition to the function of regulating the general arterial pressure the cardio-aortic and carotid sinus nerves act as the buffer or moderator nerves of the blood pressure. Heymans demonstrated in dogs that functional suppression of the aortic and carotid sinus nerves produces immediately an intense arterial hypertension. The degree of hypertension which develops after section of the moderator nerves depends mainly on the sympathetic vasopressor tone. In dogs total excision of the sympathetic paravertebral ganglionic chains prevents or causes the disappearance of this type of experimental hypertension. This experimental form is not the same as clinical nephropathic hypertension. It resembles more the so-called neurogenic hypertension.

Leriche demonstrated in extensive clinical material that vasodilatation can be produced and maintained by arterial sympathectomy. Brüning in 1923 suggested sympathectomy for the control of hypertension. Adson

1. Heymans, C.: Some Aspects of Blood Pressure Regulation and Experimental Arterial Hypertension, *Surgery* 4: 487 (Oct.) 1938.

and Brown demonstrated that sympathetic ganglionectomy and trunk resection produce an increased blood flow as measured in degrees of increased elimination of heat. Freyberg and Peet sectioned the major and minor splanchnic nerves and the lower dorsal sympathetic chain subdiaphragmatically in forty-eight cases. In almost every case there was a sharp fall of blood pressure to normal or below immediately after the operation. The result was permanent in some and less permanent in others, while the blood pressure rose to the preoperative level in still others.

Goldblatt and his co-workers<sup>2</sup> produced in dogs, by applying a clamp to the renal arteries, permanent elevation of both the systolic and the diastolic pressure. In subsequent experiments these authors<sup>3</sup> demonstrated that in dogs at least the excision of the thoracic portion of the splanchnic nerves and the lower four dorsal sympathetic ganglia on both sides does not prevent, cure or permanently lower in any degree experimental renal hypertension produced by renal ischemia. The authors, however, felt that the results of their experiments did not necessarily controvert the reports of beneficial effects in some cases of human hypertension.

In a recent communication Craig<sup>4</sup> reported 158 cases of essential hypertension in which subdiaphragmatic extensive sympathectomy was practiced. The operation consisted of the resection of the major, minor and lesser splanchnic nerves, with a portion of the celiac ganglion and the removal of the upper lumbar ganglia on each side through a subdiaphragmatic approach. The operation was performed in two stages with an interval of ten days between the operations on the right and left sides. The procedure is associated with a small risk and is followed by satisfactory alleviation of symptoms in selected cases. Their observations have shown that, when the blood pressure fluctuates widely and reaches low levels at times, operation is most beneficial. But when the blood pressure is fixed in high levels surgical treatment is of little value. This emphasizes the necessity of preoperative tests to determine the flexibility of the pressure. Operation proved most efficacious in the vasospastic type of hypertension, in which sharp rises in blood pressure occur when the hands are immersed in cold water, and in cases in which a considerable fall in blood pressure is produced when sodium ethyl (1 methyl butyl) thiobarbiturate, sodium amytal or a nitrite is administered. As an average rule the patient must be under 50 years of age and the hypertension from moderate to severe with moderate sclerosis of the retinal arteries. Goldblatt<sup>5</sup> calls attention to the fact that some of the methods which were regarded as effective

at first were discarded later as useless even by the originators. He considers factors other than the level of the blood pressure, such as disappearance of headache, and other subjective symptoms, unreliable as criteria. According to Goldblatt, after all the operations the percentage of cases in which there is a return of blood pressure to normal is relatively small.

#### EQUINE ENCEPHALOMYELITIS IN BIRDS

The horse, according to a recent report by Tyzzer and his co-workers<sup>1</sup> of the Harvard Medical School, has only a minor part in the spread of equine encephalomyelitis; they suggest that the main proliferation and dissemination are by migratory birds.

Last September numerous pheasants and other wild birds were found dead or in a helpless paralytic condition in certain rural sections of Connecticut. Four moribund pheasants were sent to the Harvard Medical School for diagnosis. On account of the history of paralysis in these birds and the absence of gross lesions, brain emulsions were prepared and injected intracerebrally into Swiss mice. All mice thus injected died in from four to five days with symptoms similar to those observed in mice injected with the eastern type of horse encephalomyelitis. At necropsy the brain tissues of the mice were found to be bacteriologically sterile. Serial passage of the pheasant virus in mice was found to be possible, as many as ten mouse passages having been made with no apparent reduction in virulence. The virus was found to have an unusually high mouse infectivity, 0.2 cc. of the brain emulsion containing at least 10,000,000 minimal lethal doses.

Neutralization tests were made with a specific anti-equine encephalomyelitis rabbit serum (eastern type) obtained from the Rockefeller Institute. One cc. of this antiserum would neutralize 500,000 lethal units of the virus. The virus isolated from parietic pheasants, therefore, is apparently immunologically identical with the eastern strain of horse encephalomyelitis.

The Harvard pathologists found quail and domestic fowl susceptible to this pheasant strain. Other investigators<sup>2</sup> have proved the susceptibility of pigeons, ducks, geese, blackbirds and hawks to eastern horse encephalomyelitis. Migratory birds are thus clearly implicated in the epidemiology of this disease. Tyzzer feels therefore that the term "equine" is misleading. In his opinion the disease should be regarded as a primary "avian" infection, which under accidental circumstances or when the infection rises to a certain level "overflows" and becomes a serious problem as regards the horse and man. Much more extensive statistical evidence must be available before this suggested theory can be accepted. Confirmatory evidence in support of the theory has already been published, however, by

2. Goldblatt, Harry; Lynch, J.; Hanzal, R. F., and Summerville, W. W.: Studies on Experimental Hypertension: I. The Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemia, *J. Exper. Med.* 59: 347 (March) 1934.

3. Goldblatt, Harry; Gross, Jerome, and Hanzal, R. F.: The Effect of Resection of Splanchnic Nerves on Experimental Renal Hypertension, *J. Exper. Med.* 65: 233 (Feb.) 1937.

4. Craig, W. McK.: Essential Hypertension: The Selection of Cases Obtained by Subdiaphragmatic Extensive Sympathectomy, *Surgery* 4: 502 (Oct.) 1938.

5. Goldblatt, Harry: Experimental Observations on the Surgical Treatment of Hypertension, *Surgery* 4: 483 (Oct.) 1938.

1. Tyzzer, E. E.; Sellards, A. W., and Bennett, B. L.: *Science* 88: 505 (Nov. 25) 1938.

2. Giltner, L. T., and Shahan, M. S.: *Science* 78: 62, 1933. Remington, P., and Bailly, J.: *Compt. rend. Soc. de biol.* 120: 1067, 121: 146, 122: 518, 123: 562, 1936.

Fothergill and Dingle,<sup>3</sup> who isolated the same virus from a pigeon epidemic in southeastern Massachusetts. Other recent investigators<sup>4</sup> have emphasized the role of insect vectors in horse encephalitis. At least six species of mosquitoes can be infected with the horse virus and can transmit the disease to laboratory animals; but infected mosquitoes have never been found in nature. The high infectivity of mice to nasal instillation with the virus suggest that smaller rodents may also be implicated.

## Current Comment

### PERPETUATION OF ERRORS IN MEDICAL BIBLIOGRAPHY

In checking the older references in medical periodicals, one not infrequently finds errors in the cited source or in the statement attributed to that source. One of the most astonishing examples has been recently published by Dobell<sup>1</sup> in an article entitled "Dr. O. Uplavici (1887-1938)." In January 1887 a paper was published by the late Dr. Jaroslav Hlava in the *Časopis lékařův českých* (Journal of the Czech Physicians) recording his discovery of amebas in the stools and intestinal ulcers of patients suffering from dysentery. He also reported success in causing dysentery in cats by the intrarectal inoculation of dysenteric stools. Dr. Hlava was professor of pathologic anatomy at Prague. While his paper of 1887, written wholly in the Czech language, was entitled "O úplavici, Předběžné sdělení," meaning "On Dysentery: Preliminary Communication," the original became known to most workers through a brief review in German signed by the late Dr. Stephanos Kartulis of Alexandria. By some extraordinary mistake the author's name (Hlava) was entirely omitted and the title of the paper was given in its place as "Uplavici, O." Kartulis in fact referred to the author personally as "Uplavici" and even mentions correspondence with a man of this peculiar name. In the contents of the *Centralblatt* in which Hlava's paper was abstracted the author's name is given as "Uplavici, O." In the subject index the name appears as "Hlava, Uplavici," but in the author index "Hlava" is the only entry, "Uplavici" having vanished without any explanation. The result has been that over the intervening years the authorship of this paper has been assigned variously to "O. Hlava" (instead of J. Hlava), to "Hlava, Uplavici" (as though Uplavici were Hlava's forename) and to "O. Hlava (O. Uplavici)" as though the two names were synonymous; in fact in a recent paper both Hlava and Uplavici are mentioned as though two different authorities had studied dysentery in cats in early days. Finally in the Index Catalogue of Medical and Veterinary Zoology Hlava's paper is first indexed with the wrong initial "O" but it is also attributed, without any explanation, to "Uplavici, O." and this name is followed by the further information "Dr." (in square brackets). As announced by Dobell, "Dr. O. Uplavici"

is finally dead. Doubtless, however, other extraordinary bibliographic errors remain in medical periodical literature awaiting the day when some meticulous investigator will bring them to light.

## VITAMIN K

Early in 1937 *THE JOURNAL*<sup>1</sup> discussed the discovery of vitamin K and the results of the earlier experimental work in connection with this food factor. Several investigators have commented either on the occurrence of hemorrhages and prolonged bleeding developing in persons on purified diets or on the exceptional efficacy of certain foods in promoting the clotting of blood; these foods are now considered good sources of vitamin K. The present view is that this food factor is instrumental in maintaining the level of prothrombin in the blood. The hemorrhage is usually traumatic in origin, but diminished prothrombin results in a prolongation of clotting time which emphasizes the seriousness of the hemorrhage. Along with the prolonged clotting time in chicks is an anemia which likewise responds to vitamin K given in the form of an extract of alfalfa.<sup>2</sup> Bile is highly important in facilitating the utilization of vitamin K probably by promoting its absorption; this has now been shown in rats,<sup>3</sup> in dogs<sup>4</sup> and in human patients.<sup>5</sup> In clinical obstructive jaundice the low prothrombin level in the blood is raised by restoring bile to the intestine, but the effect is much more striking if both vitamin K and bile are used. In recent studies on chicks a definite parallelism between allowance of vitamin K concentrate and duration of restored normal clotting time has been shown.<sup>6</sup> The chemical nature of effective concentrates has been variously described as a nonsterol oil or waxy solid containing one or more benzene rings but no hydroxyl or ketone groups and particularly subject to destruction by sunlight, alkali and adsorption on aluminum oxide or magnesium oxide. It is said that it does not contain sulfur or phosphorus. A recent report<sup>7</sup> describes a crystalline product prepared from alfalfa leaves and so potent that 0.6 microgram will reduce the clotting time of 50 per cent of a large number of hemorrhagic chicks to normal. The crystals melt at 69 C. and loss in potency did not occur on recrystallization from various solvents. A still more recent report<sup>8</sup> describes an active clotting factor prepared from dog, pig and lamb livers; this, however, gave chemical evidence of being a sterol. The astonishing progress made during the past three years since the existence of a food factor which is important in blood clotting was first established shows the extent to which the conception of deficiency diseases has become a part of medical philosophy.

1. Antihemorrhagic Factor in Foods, editorial, J. A. M. A. 108: 1717 (May 15) 1937.

2. Thayer, S. A.; McKee, R. W.; MacCorquodale, D. W., and Doisy, E. A.: *Proc. Soc. Exper. Biol. & Med.* 37: 417 (Nov.) 1937.

3. Greaves, J. P., and Schmidt, C. L. A.: *Proc. Soc. Exper. Biol. & Med.* 37: 43 (Oct.) 1937.

4. Smith, H. P.; Warner, E. D.; Brinkhous, K. M., and Seegers, W. H.: *J. Exper. Med.* 67: 911 (June) 1938.

5. Butt, H. R.; Snell, A. M., and Osterberg, A. E.: *Proc. Staff Meet., Mayo Clin.* 13: 74 (Feb. 2) 1938. Warner, E. D.; Brinkhous, K. M., and Smith, H. P.: *Proc. Soc. Exper. Biol. & Med.* 37: 623 (Jan.) 1938.

6. Ansbacher, S.: *Science* 88: 221 (Sept. 2) 1938.

7. Thayer, S. A.; MacCorquodale, D. W.; Binkley, S. B., and Doisy, E. A.: *Science* 88: 243 (Sept. 9) 1938.

8. Lichtman, A. L., and Chambers, W. H.: *Science* 88: 358 (Oct. 14) 1938.

3. Fothergill, Le Roy D., and Dingle, John H.: *Science* 88: 549 (Dec. 9) 1938.

4. Eklund, C. M., and Blumstein, Alex.: *The Relation of Human Encephalitis to Encephalomyelitis in Horses*, J. A. M. A. 111: 1734 (Nov. 5) 1938.

1. Dobell, Clifford: *Parasitology* 30: 239 (June) 1938.

# ORGANIZATION SECTION

## INDICTMENT OF THE AMERICAN MEDICAL ASSOCIATION

Following is the complete text of the indictment of the American Medical Association and other defendants in the District of Columbia.

DISTRICT COURT OF THE UNITED STATES FOR THE DISTRICT OF COLUMBIA HOLDING A CRIMINAL TERM

October Term, A. D. 1938

UNITED STATES OF AMERICA,  
DISTRICT OF COLUMBIA, ss:  
INDICTMENT

THE GRAND JURORS of the United States of America, at a regular term of the District Court of the United States for the District of Columbia, to wit: the October 1938 term thereof, held at Washington, in the District of Columbia, after being duly impaneled, sworn and charged at the term of court aforesaid, as an additional Grand Jury in and for said District, inquiring for the said District, upon their oaths find and present, as follows:

### I. THE DEFENDANTS

1. The following corporations and associations are hereby made defendants:

- (1) American Medical Association, incorporated under the laws of Illinois and having its office and principal place of business in Chicago, Illinois;
- (2) The Medical Society of the District of Columbia, incorporated under an Act of Congress and having its office and principal place of business in the District of Columbia;
- (3) Harris County Medical Society, an unincorporated association, having its office and its principal place of business in Houston, Harris County, Texas;
- (4) Washington Academy of Surgery, an unincorporated association, having its office and its principal place of business in the District of Columbia.

2. The following individuals, who will be referred to hereinafter as "the individual defendants," are hereby made defendants:

Arthur Carlisle Christie	Thomas Edwin Neill
Coursen Baxter Conklin	Edward Hiram Reede
James Bayard Gregg Custis	William Mercer Sprigg
William Dick Cutter	William Joseph Stanton
Morris Fishbein	John Ogle Warfield Jr.
Thomas Allen Groover	Olin West
Robert Arthur Hooe	Prentiss Willson
Rosco Genung Leland	William Creighton Woodward
Leon Alphonse Martel	Wallace Mason Yater
Thomas Ernest Mattingly	Joseph Rogers Young
Francis Xavier McGovern	

### II. THE WASHINGTON HOSPITALS

3. Each of the following corporations and associations were engaged in the business of operating a hospital throughout the period of the conspiracy hereinafter described:

Central Dispensary and Emergency Hospital  
Children's Hospital of the District of Columbia  
Columbia Hospital for Women  
Eastern Dispensary and Casualty Hospital  
Episcopal Eye, Ear and Throat Hospital  
Garfield Memorial Hospital  
Georgetown University Hospital  
George Washington University Hospital  
National Homeopathic Hospital of the District of  
Providence Hospital  
Sibley Memorial Hospital  
Washington Sanitarium and Hospital

These hospitals are located in Washington in the District of Columbia, except that the Washington Sanitarium and Hospital is located in Takoma Park, Maryland. The hospitals listed in this paragraph will be referred to collectively hereinafter as

"the Washington hospitals." The said hospitals include all of the hospitals in the District of Columbia not operated by the government.

### III. RELATIONSHIP BETWEEN CERTAIN DEFENDANTS

A. *Relationship Between Defendant American Medical Association and Defendants The Medical Society of the District of Columbia and Harris County Medical Society.*

4. Membership in defendant American Medical Association is ordinarily obtainable only through affiliated state or territorial medical associations, known as "constituent" associations or societies of American Medical Association. Defendant The Medical Society of the District of Columbia is a constituent medical society of defendant American Medical Association. Membership in most "constituent" associations or societies is ordinarily obtainable only through membership in affiliated county or local medical societies, known as "component" societies of those constituent associations and of the American Medical Association. Defendant The Medical Society of the District of Columbia has no component societies. Defendant Harris County Medical Society is a component medical society of defendant American Medical Association. Members of affiliated component or constituent medical societies are, *ipso facto*, members of defendant American Medical Association.

B. *Memberships and Offices Held by Individual Defendants.*

5. Membership in defendant American Medical Association was held by all individual defendants throughout the period of the conspiracy hereinafter described. For many years, and throughout the period of the conspiracy hereinafter described, the following individual defendants, namely:

Morris Fishbein, Editor of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION;  
Olin West, Secretary and General Manager of the American Medical Association;  
William Creighton Woodward, Director of the Bureau of Legal Medicine and Legislation of the American Medical Association;  
William Dick Cutter, Secretary of the Council on Medical Education and Hospitals of the American Medical Association;  
Rosco Genung Leland, Director of the Bureau of Medical Economics of the American Medical Association,

have been employed by defendant American Medical Association in the positions indicated and, as the principal full-time officials and employees of said defendant Association, have been engaged in the active management of its business affairs and have been largely instrumental in forming and effectuating its policies and, in particular, in managing the business affairs and in forming and effectuating the policies of said defendant Association hereinafter set forth.

6. Membership in defendant The Medical Society of the District of Columbia was held, throughout the period of the conspiracy hereinafter described, by all of the individual defendants except those listed in paragraph 5 of this indictment as employees and officials of defendant American Medical Association.

7. Defendant The Medical Society of the District of Columbia has an executive committee charged with carrying out the policies of the said defendant society.

8. Offices in defendant The Medical Society of the District of Columbia, and membership on the Executive Committee, were held during all or part of the period of the conspiracy hereinafter described by the individual defendants whose names are indicated below:

Thomas Edwin Neill, President, and member of the Executive Committee;  
Coursen Baxter Conklin, Secretary-Treasurer, and member of the Executive Committee;  
Robert Arthur Hooe, member of the Executive Committee;

Francis Xavier McGovern, member of the Executive Committee;

Edward Hiram Reede, member of the Executive Committee;  
William Mercer Sprigg, member and Chairman of the Executive Committee;

Wallace Mason Yater, member of the Executive Committee.

9. Membership on the Hospital Committee of defendant The Medical Society of the District of Columbia was held by the individual defendants listed below during all or part of the period of the conspiracy hereinafter described:

Leon Alphonse Martel

John Ogle Warfield Jr.

Joseph Rogers Young

10. Membership on regular or attending staffs of the Washington hospitals was held by individual defendants throughout the period of the conspiracy hereinafter described, as follows:

Courson Baxter Conklin

Children's Hospital of the District of Columbia

Eastern Dispensary and Casualty Hospital

George Washington University Hospital

James Bayard Gregg Custis

National Homeopathic Hospital of the District of Columbia

Robert Arthur Hooe

Central Dispensary and Emergency Hospital

Thomas Ernest Mattingly

Sibley Memorial Hospital

Leon Alphonse Martel

Georgetown University Hospital

Francis Xavier McGovern

Garfield Memorial Hospital

Thomas Edwin Neill

Episcopal Eye, Ear and Throat Hospital

Garfield Memorial Hospital

William Mercer Sprigg

Columbia Hospital for Women

William Joseph Stanton

Georgetown University Hospital

John Ogle Warfield Jr.

Children's Hospital of the District of Columbia

Garfield Memorial Hospital

Prentiss Willson

Columbia Hospital for Women

Wallace Mason Yater

Georgetown University Hospital

Joseph Rogers Young

Eastern Dispensary and Casualty Hospital

#### IV. THE BACKGROUND OF THE CONSPIRACY

11. In the last few decades great and unprecedented advances in medical knowledge and technic have occurred. No single doctor now knows or can know enough medical science to enable him to render complete and adequate medical care. Specialization in the rendition of medical care has necessarily resulted. Costly diagnostic and therapeutic equipment and facilities have now become essential for the rendition of complete and adequate medical care. The cost of complete and adequate medical care has increased substantially.

12. Many persons embraced within the low income group in the United States, including the District of Columbia, do not now obtain, and cannot now afford to obtain, complete and adequate medical care.

13. During the last few decades, many general practitioners and specialists have associated themselves together in group practice in order to reduce the cost and improve the quality of medical care by sharing their knowledge and by making joint use of equipment and facilities. During the last few decades attempts have been made to enable persons in the low income group to meet the cost of medical care on a risk sharing prepayment basis and thus to avoid excessive economic burdens occasioned by the uneven incidence of illness. To achieve these objectives, organizations have been formed in which general practitioners and specialists engaged in group practice undertake to give complete medical care of high quality to persons who pay therefor on a risk sharing prepayment basis.

14. Experimentation with group medical practice on a risk sharing prepayment basis, if not obstructed by coercive restraints, may contribute to the solution of the problem of providing

complete and adequate medical care. Many surveys of the problem in recent years have resulted in recommendations for such experimentation. There is reason to believe, and a large body of informed opinion holds, that the supplying of medical care in this manner and on this basis may be so organized as to obtain qualified doctors and to afford those doctors conditions of practice which are conducive to a high quality of medical service satisfactory to both doctor and patient and which enable the said doctors to find satisfaction in their work and to obtain a stable, adequate net income; moreover, that this method of supplying medical care may be utilized without unduly affecting such free choice of physicians as is ordinarily enjoyed by patients and without involving interference on the part of laymen with the medical service or with the relationship subsisting between doctor and patient. There is reason to believe, and a large body of informed opinion holds, that such method of providing medical care is less costly than, and, in many respects from the standpoint of both doctor and patient, superior to, individual practice on a fee for service basis.

15. Principally for economic reasons and because it has feared, for its members, business competition from the doctors connected with organizations in which doctors engage in group practice on a risk sharing prepayment basis, defendant American Medical Association, and the individual defendants employed by said defendant Association, have adopted and for many years have pursued a policy of opposition to experimentation with such organizations, and have taken affirmative steps to oppose their formation and operation throughout the United States.

#### V. THE DOMINANT POSITION OF DEFENDANT AMERICAN MEDICAL ASSOCIATION AND THE CIRCUMSTANCES AFFORDING THE DEFENDANTS, ACTING TOGETHER, ECONOMIC AND OTHER COERCIVE POWER TO RESTRAIN GROUP MEDICAL PRACTICE ON A RISK SHARING PREPAYMENT BASIS

##### A. The Importance of Membership in Medical Societies, of Consultations and of Hospital Privileges.

16. Membership in a medical society affiliated with defendant American Medical Association, and hence in defendant American Medical Association itself, is valuable to practicing doctors because such membership carries professional prestige, because defendant American Medical Association and affiliated societies provide desirable services for and contacts to members, and because many doctors and many hospitals and others serving the medical profession deal only with such doctors as are members of defendant American Medical Association. Exclusion or expulsion from membership in a medical society affiliated with defendant American Medical Association, and hence from membership in defendant American Medical Association itself, deprives doctors, including doctors engaged in group practice on a risk sharing prepayment basis, of these advantages and also injures their professional standing.

17. Consultations between doctors are frequently advantageous, both to the patient and to the doctors. Defendant American Medical Association recommends that doctors seek consultations with other doctors in cases of serious illness. Consultations with specialists outside of the group is frequently desirable for doctors engaged in group practice on a risk sharing prepayment basis. Doctors, including doctors engaged in group practice on a risk sharing prepayment basis, are seriously handicapped if they are prevented from obtaining consultations.

18. The privilege of attending and treating their patients in a well equipped hospital is essential for all practicing surgeons. Such privilege is desirable for all practicing doctors. Exclusion from hospitals of surgeons and physicians, including those engaged in group practice on a risk sharing prepayment basis, seriously restrains them in the pursuit of their callings.

19. It is desirable and frequently essential for the successful conduct of the business of organizations engaged in arranging for the provision of medical care by salaried doctors engaged in group medical practice on a risk sharing prepayment basis, and thus for the members of or subscribers to such organizations, that the doctors composing the medical staffs thereof, equally with other doctors, be afforded the opportunity of

obtaining, and be not prevented from obtaining, memberships in medical societies, consultations with other doctors, and the use of hospital facilities.

*B. Power of Certain Defendants to Exclude and to Expel Doctors Engaged in Group Practice on a Risk Sharing Prepayment Basis from Membership in Medical Societies.*

20. A large percentage of the doctors practicing in the District of Columbia (in excess of 800) are members of defendant The Medical Society of the District of Columbia, and thus of defendant American Medical Association. There are approximately 145,000 doctors engaged in practice in the United States. Approximately 110,000 doctors are members of defendant American Medical Association. Defendant American Medical Association has a gross income of several million dollars a year, and its investments in capital assets have been and are substantial; it employs about 500 persons in the conduct of its business. Defendant American Medical Association is engaged in the business of publishing a weekly magazine known as THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, which has a weekly circulation of approximately 95,000; it is the only medical journal with an extensive circulation among the members of the medical profession. The said JOURNAL contains a section entitled "Organization Section," devoted to organizational, business, economic and social aspects of medical practice. The said JOURNAL has been edited and managed in such a manner as to express the policy of defendant American Medical Association and of the individual defendants employed by it of opposition to group medical practice on a risk sharing prepayment basis and to further the effectuation of such policy of opposition. The columns of said JOURNAL have not been open for the expression of contrary views about group medical practice on a risk sharing prepayment basis. Defendant American Medical Association maintains a bureau known as the Bureau of Medical Economics, which concerns itself with the economic organization of the practice of medicine. The said Bureau of Medical Economics has taken a leading part in carrying out defendant American Medical Association's policy of opposing, discouraging and suppressing group medical practice on a risk sharing prepayment basis. By reason of its size, organization and activities, defendant American Medical Association is the only important society representative of the medical profession in the United States. The medical profession in the United States and its policies are influenced and to a great extent controlled by defendant American Medical Association.

21. Defendant American Medical Association has promulgated certain rules, called by it "Principles of Medical Ethics," which purport to define the duties of doctors in their relations with their patients and among themselves. The constituent and component societies of defendant American Medical Association, including defendant The Medical Society of the District of Columbia and defendant Harris County Medical Society, have adopted and they govern their members by the said "Principles of Medical Ethics." The members of defendant The Medical Society of the District of Columbia are required to, and do, pledge themselves to comply with said principles. These so-called "Principles of Medical Ethics" are expressed in the form of indefinite standards and, as interpreted and applied by defendant American Medical Association and its affiliated constituent and component societies, are not confined to requirements of ethical, moral or legal conduct but embody as well purely economic restrictions upon the practice of medicine. Under these rules, so interpreted, defendant American Medical Association and its affiliated constituent and component societies can, and frequently do, condemn as "unethical" group medical practice on a risk sharing prepayment basis, principally because such practice is in business competition with and threatens the incomes of doctors engaged in practice on a fee for service basis, and particularly of doctors so practicing who are members of defendant American Medical Association and its affiliated constituent and component societies.

22. The affiliated, constituent and component societies of defendant American Medical Association, including defendant

The Medical Society of the District of Columbia and defendant Harris County Medical Society, act as enforcing agencies of defendant American Medical Association with respect to the "Principles of Medical Ethics." Said constituent and component societies, including defendant The Medical Society of the District of Columbia and defendant Harris County Medical Society, under the supervision and control of defendant American Medical Association, have the power to, and do, suspend, expel or otherwise discipline members claimed by said defendant societies and association to have violated the "Principles of Medical Ethics." Principally for the reasons hereinabove set forth, defendants American Medical Association, The Medical Society of the District of Columbia and Harris County Medical Society possess power to expel or exclude from membership a doctor disapproved by them solely because he has associated himself with group medical practice on a risk sharing prepayment basis.

*C. Power of Certain Defendants to Restrain Doctors from Engaging in Group Medical Practice on a Risk Sharing Prepayment Basis and to Restrain Doctors from Consulting with Doctors so Engaged.*

23. A provision, to wit: Chapter IX, Article IV, Section 5 of the constitution of defendant The Medical Society of the District of Columbia prohibits any professional relationship whatsoever, including consultations, between members of the said defendant Society on the one hand and, on the other, any doctor, organization or group rendering medical care within the District of Columbia or within ten miles thereof, which doctor, organization or group has not been "approved" by defendant The Medical Society of the District of Columbia. By reason of this provision, and by reason of the power of defendant The Medical Society of the District of Columbia to exclude applicants for membership, and to suspend, expel or otherwise discipline its members, under the supervision and control of defendant American Medical Association, said defendants have power to deter doctors from engaging in group medical practice on a risk sharing prepayment basis or from consulting with doctors engaged in such group practice.

*D. Power of Certain Defendants to Restrain Doctors Engaged in Group Practice on a Risk Sharing Prepayment Basis from Obtaining Access to Hospital Facilities.*

24. The medical services and the determination of the medical policies of the Washington hospitals are controlled in each such hospital by a medical staff, consisting of doctors appointed thereto by the governing body of the hospital and commonly designated as the "regular" or "attending" staff of the hospital. Doctors on such a "regular" or "attending" staff of a Washington hospital are privileged to treat and operate upon their private patients within that hospital and to use the facilities thereof. Each Washington hospital also has a "courtesy" staff, comprising those doctors, not on its "regular" or "attending" staff, who are permitted to treat or operate on their patients in that hospital. Except in emergency cases, only those doctors who have been appointed to the "attending" or "regular" staff or to the "courtesy" staff of a Washington hospital are permitted to treat or operate on patients within that hospital. Formal appointment to the courtesy staff of each Washington hospital is made by the governing body of that hospital.

25. Applications for appointment to the courtesy staff of each Washington hospital are passed upon by the attending or regular staff of that hospital. Each Washington hospital, acting through its governing body, ordinarily finds it expedient to follow, and ordinarily does follow, the recommendations of its attending or regular staff with respect to appointments to its courtesy staff. Nearly all members of the attending or regular staff of each Washington hospital are members of defendant The Medical Society of the District of Columbia and of defendant American Medical Association. As such members, they know, and can and do communicate to the Washington hospitals, the policies and wishes of defendant The Medical Society of the District of Columbia and of defendant American Medical Association.

26. Defendant The Medical Society of the District of Columbia has a standing committee, known as the Hospital Committee,



composed of a member of the regular or attending staff of each Washington hospital, whose function it is to communicate to the Washington hospitals the policies and wishes of defendant The Medical Society of the District of Columbia, to endeavor to obtain compliance by the Washington hospitals with those wishes and policies, and further, to keep defendant The Medical Society of the District of Columbia informed with respect to compliance by the Washington hospitals with those wishes and policies.

27. Defendant The Medical Society of the District of Columbia has approved each of the Washington hospitals located in Washington. Defendant The Medical Society of the District of Columbia, by withdrawing its approval of a Washington hospital, makes a member of the attending or regular medical staff of that hospital who continues to serve on such staff subject to disciplinary action by said defendant society, including expulsion from said society. Simultaneous withdrawal of the members of its regular or attending staff from a Washington hospital, in order to obtain compliance by that hospital with the wishes and policies of the defendant The Medical Society of the District of Columbia, would deprive the hospital of services essential to it, would cause it a loss of prestige and would thereby seriously injure the said hospital.

28. Defendant Washington Academy of Surgery makes recommendations to some of the Washington hospitals with respect to appointments to their courtesy staffs. In making such recommendations, defendant Washington Academy of Surgery can and does carry out the policies and wishes of defendant The Medical Society of the District of Columbia. The recommendations of defendant Washington Academy of Surgery with respect to such appointments are ordinarily followed by the regular or attending staff of the Washington hospitals in making recommendations to the governing bodies of such hospitals with respect to applications for such appointments.

29. Medical students and doctors receiving postgraduate training in hospitals, ordinarily known as "interns" and "residents," render valuable services to the hospitals without substantial compensation. Defendant American Medical Association, by means of periodic inspections, determines and declares what hospitals in the United States it believes are suitable for postgraduate training of interns and residents. No other public or private agency rates hospitals for this purpose. In order to obtain credit generally throughout the medical profession for postgraduate training in hospitals, and frequently in order to obtain a medical degree or a license to practice, it is necessary for medical students and doctors to take such training in hospitals which defendant American Medical Association has approved for that purpose. Loss of approval by defendant American Medical Association therefore not only causes a loss of prestige to a hospital but also ordinarily prevents a hospital from obtaining interns and residents. Inability to obtain interns and residents ordinarily compels a hospital to employ house doctors, at substantial expense.

30. Defendant American Medical Association has adopted the policy that hospitals approved by it for intern and resident training should have on their medical staffs only doctors who are members of defendant American Medical Association.

31. Each Washington hospital is approved by defendant American Medical Association for the training of interns or of residents or of both. The power of defendant American Medical Association to withdraw such approval gives defendant American Medical Association power to enforce compliance by Washington hospitals with the policies and wishes of defendant The Medical Society of the District of Columbia and of defendant American Medical Association.

32. Principally for the reasons hereinabove alleged defendants American Medical Association, The Medical Society of the District of Columbia, and Washington Academy of Surgery possess power to expel or exclude a doctor, disapproved by them solely because he has engaged in group medical practice on a risk sharing prepayment basis, from attending and treating his patients in the Washington hospitals, the said Washington hospitals including all the hospitals in the District of Columbia in which private patients may be treated by doctors.

## VI. THE CONSPIRACY

33. Group Health Association, Inc., was incorporated on February 19, 1937, and authorized to do business under and by virtue of the laws of Congress for the District of Columbia. Said corporation is a non-profit, cooperative association of employees of certain departments in the executive branch of the United States Government employed in the District of Columbia. Most members of Group Health Association, Inc., are embraced within the low income group, over 80 per cent of them earning annual incomes of not more than \$2,000. Said corporation is engaged in the District of Columbia in the business of arranging for the provision of medical care and hospitalization to its members and their dependents on a risk sharing prepayment basis. Said corporation collects monthly payments in the form of dues from its members. Medical care is provided by a medical staff consisting of salaried general practitioners and specialists engaged in group practice under the sole direction of a medical director. Said corporation pays adequate salaries to the doctors on its medical staff and provides the medical staff with a modern, well equipped clinic, which was opened on November 1, 1937. Said corporation also defrays, within limits, the expenses of hospitalization of its members and their dependents. The personal relationship ordinarily existing between doctor and patient obtains between the doctors on the medical staff of Group Health Association, Inc., and their Group Health Association, Inc., patients.

34. Beginning in January 1937, or shortly thereafter, and continuing to the date of the presentation of this indictment, the defendants, and certain members of defendant The Medical Society of the District of Columbia not made defendants, and the Washington hospitals, and other persons to the grand jurors unknown, well knowing the foregoing facts, have combined and conspired together for the purpose of restraining trade in the District of Columbia, that is to say:

- (1) for the purpose of restraining Group Health Association, Inc., in its business of arranging for the provision of medical care and hospitalization to its members and their dependents on a risk sharing prepayment basis;
- (2) for the purpose of restraining the members of Group Health Association, Inc., in obtaining, by cooperative efforts, adequate medical care for themselves and their dependents from doctors engaged in group medical practice on a risk sharing prepayment basis;
- (3) for the purpose of restraining the doctors serving on the medical staff of said Group Health Association, Inc., in the pursuit of their callings;
- (4) for the purpose of restraining doctors (not on the medical staff of Group Health Association, Inc.) practicing in the District of Columbia, including the doctors so practicing who are made defendants herein, in the pursuit of their callings;
- (5) for the purpose of restraining the Washington hospitals in the business of operating such hospitals.

In so doing, defendants have then and there engaged in an unlawful combination and conspiracy in restraint of trade in and of the District of Columbia in violation of Section 3 of the Act of Congress on July 2, 1890, known as the Sherman Antitrust Act.

35. Throughout the period covered by this indictment, Group Health Association, Inc., and its medical staff were discussed at frequent meetings of defendant The Medical Society of the District of Columbia and of committees of said defendant Society, and at other meetings and conferences. At such meetings and conferences, the combination and conspiracy hereinabove described was proposed, discussed and formed, in part, and carried on in part. Plans, understandings and agreements to accomplish the unlawful purposes hereinabove described were proposed, discussed and adopted at such meetings. Many of such plans, understandings and agreements were set forth in formal resolutions adopted by defendant The Medical Society of the District of Columbia, and by the committees thereof. Among such resolutions was the following resolution adopted

at a meeting of defendant The Medical Society of the District of Columbia, held in Washington in the District of Columbia on November 3, 1937:

WHEREAS, The Medical Society of the District of Columbia has an apparent means of hindering the successful operation of Group Health Association, Inc., if it can prevent patients of physicians in its employ being received in the local private hospitals; and

WHEREAS, The Medical Society of the District of Columbia has no direct control over the policies of such hospitals as determined by their lay boards of directors, except through its control of its own members serving on their medical staffs; and

WHEREAS, conflicts between the Medical Society of the District of Columbia and any local hospitals arising from an attempt to enforce the provisions of Chapter IX, Article IV, Section 5, of its Constitution should be assiduously avoided, if possible, because of the unfavorable publicity that would accrue to its own members; therefore, be it

Resolved, That the Hospital Committee be, and is hereby directed to give careful study and consideration to all phases of this subject and report back to the Society, at the earliest practicable date, its recommendations as to the best way of bringing this question to the attention of the medical boards and boards of directors of the various local hospitals in such a manner as to insure the maximum amount of practical accomplishment with the minimum amount of friction and conflict.

Following adoption of the said resolution of November 3, 1937, the combination and conspiracy hereinabove described was further discussed and carried on at later meetings of defendant The Medical Society of the District of Columbia and of committees of said defendant Society, and at other meetings and conferences. Said meetings were held, said resolutions were adopted, and said plans, understandings and agreements were proposed, discussed and adopted, with the knowledge, approval and assistance of defendant American Medical Association and of the individual defendants who are employed by defendant American Medical Association.

36. The combination and conspiracy hereinabove described and the intended restraints which have resulted therefrom have been effectuated in the following manner and by the following means, among others, to wit:

- (a) Defendants have combined and conspired with the plan and purpose to hinder and obstruct Group Health Association, Inc., in procuring and retaining on its medical staff qualified doctors, and to hinder and obstruct the doctors serving on that staff from obtaining consultations with other doctors and specialists practicing in the District of Columbia. Pursuant to this plan and purpose the defendants have performed, among others, the following acts: Defendants (other than defendants Washington Academy of Surgery and Harris County Medical Society) circulated a "white list" of organizations, groups and individuals approved by defendant The Medical Society of the District of Columbia, omitting from said "white list" the name of Group Health Association, Inc., with the intent and purpose of threatening with disciplinary action any doctors, members of defendant The Medical Society of the District of Columbia, who should become members of the medical staff of Group Health Association, Inc., or who should consult with members of the medical staff of Group Health Association, Inc. Defendants (other than defendants Washington Academy of Surgery and Harris County Medical Society) instituted disciplinary proceedings against two doctors, who were the only doctors on the medical staff of Group Health Association, Inc., who were members of defendant The Medical Society of the District of Columbia. Principally by means of such disciplinary proceedings, the said defendants induced and coerced one of the said doctors to resign from the staff of Group Health Association, Inc., and brought about the expulsion of the other doctor from membership in defendant The Medical Society of the District of Columbia. Defendant Harris County Medical Society at the request of defendant The Medical Society of the District of Columbia and of the other defendants (except defendant Washington Academy of Surgery), instituted disciplinary proceedings against a doctor on the medical staff of Group Health Association, Inc., who was a member in good standing of said defendant Harris County Medical Society and the only other

doctor on the medical staff of Group Health Association, Inc., who was a member of defendant American Medical Association. The doctors against whom the above described disciplinary proceedings were instituted were and are qualified, ethical doctors in good standing; the disciplinary proceedings above described were instituted against these doctors because of their association with Group Health Association, Inc., and for the purpose of depriving the said Group Health Association, Inc., doctors of the privileges of consulting with other doctors and of using the facilities of the Washington hospitals. The said defendants also instituted similar disciplinary proceedings against a specialist practicing medicine in the District of Columbia, on the alleged ground that he had consulted with a doctor on the staff of Group Health Association, Inc., intending thereby to penalize the said specialist for failing to boycott Group Health Association, Inc., doctors and thereby to induce other specialists to boycott Group Health Association, Inc., doctors. Principally by the means hereinabove described, defendants have coerced doctors to boycott Group Health Association, Inc., by refraining from becoming members of or by resigning from the medical staff of Group Health Association, Inc., and to boycott doctors on the medical staff of Group Health Association, Inc., by refusing to consult with them about their patients. By thus coercing doctors, defendants hindered and obstructed Group Health Association, Inc., in procuring and retaining on its medical staff qualified doctors, and hindered and obstructed doctors on the medical staff of Group Health Association, Inc., in obtaining consultations with doctors not on that staff.

- (b) Defendants have combined and conspired with the plan and purpose to hinder and obstruct Group Health Association, Inc., in obtaining access to hospital facilities for its members, and to hinder and obstruct the doctors on the medical staff of Group Health Association, Inc., from treating and operating upon their patients in Washington hospitals. Pursuant to this plan and purpose, defendants have performed, among others, the following acts: Defendants (other than defendants Washington Academy of Surgery and Harris County Medical Society) circulated among the Washington hospitals a "white list" of organizations, groups and individuals approved by defendant The Medical Society of the District of Columbia, omitting from said "white list" the name of Group Health Association, Inc., with the intent and purpose of threatening with punitive action any such hospital which should admit to its courtesy staff a doctor on the medical staff of Group Health Association, Inc., however qualified or however great his professional skill. Defendants (other than defendants Washington Academy of Surgery and Harris County Medical Society) urged and demanded that the Washington hospitals admit to their staffs only those doctors who were members of defendant The Medical Society of the District of Columbia or of neighboring medical societies affiliated with defendant American Medical Association and, hence, of defendant American Medical Association, well knowing that doctors on the medical staff of Group Health Association, Inc., were not permitted, and intending that they be not permitted, to become or remain members of such societies. Defendant Washington Academy of Surgery recommended to those Washington hospitals which made inquiry of it that said hospitals exclude from their courtesy staffs the surgeon on the medical staff of Group Health Association, Inc.; in so doing, said defendant Washington Academy of Surgery based its action principally upon the membership of said surgeon on the medical staff of Group Health Association, Inc. The Washington hospitals have failed and refused to appoint the surgeon on the medical staff of Group Health Association, Inc., to their courtesy staffs

notwithstanding the fact that said surgeon is qualified and competent in the practice of surgery; in so doing, the said hospitals based their actions principally upon the membership of said surgeon on the medical staff of Group Health Association, Inc. Defendants (other than defendants Washington Academy of Surgery and Harris County Medical Society), by threatening to deprive him of courtesy staff privileges at a Washington hospital, induced a physician on the medical staff of Group Health Association, Inc., to resign from the said Association's medical staff. Principally by the means hereinabove described, defendants have coerced the Washington hospitals to boycott Group Health Association, Inc., and the doctors on the said Association's staff. By thus coercing the Washington hospitals, defendants hindered and obstructed Group Health Association, Inc., in obtaining access to hospital facilities for its members and hindered and obstructed the doctors on the medical staff of Group Health Association, Inc., from treating and operating upon their patients in the Washington hospitals.

37. Some defendants have performed certain of the acts herein set forth in the formation and in the furtherance of the combination and conspiracy, while other defendants have performed other of the acts herein set forth in the formation and in the furtherance of the combination and conspiracy. Each defendant has, however, knowingly participated in the formation and furtherance of the combination and conspiracy, pursuant to the common purposes set forth in paragraph 34 of this indictment.

38. The combination and conspiracy hereinabove described, effectuated in part in the manner and by the means hereinabove alleged, has, as intended by defendants, prevented doctors from becoming or remaining members of the medical staff of Group Health Association, Inc., and has prevented other doctors from consulting with the doctors on the medical staff of Group Health Association, Inc., and has prevented doctors on the medical staff of Group Health Association, Inc., from treating and operating on their patients in any of the hospitals in or near the District of Columbia. Principally by these means, defendants, in thus combining and conspiring, have substantially accomplished all the illegal purposes set forth in paragraph 34 of this indictment and have succeeded in imposing all said intended restraints of trade.

#### VII. JURISDICTION AND VENUE

39. The combination and conspiracy herein set forth has been formed to a large extent and, as intended by the defendants, has operated and been carried out to a large extent, within the District of Columbia. Most of the restraints of trade resulting from such combination and conspiracy have been imposed and effected in the District of Columbia. Among other acts done in the District of Columbia for the purpose of effectuating the combination and conspiracy alleged in this indictment was the adoption of the resolution set forth in paragraph 35 of this indictment, at a meeting of defendant The Medical Society of the District of Columbia.

And so the Grand Jurors aforesaid, upon their oaths aforesaid, do find and present that defendants, throughout the period aforesaid, at the places, and in the manner and form aforesaid, unlawfully have engaged in a continuing combination and conspiracy in restraint of the aforesaid trade and commerce in and of the District of Columbia; contrary to the statute in such case made and provided, and against the peace and dignity of the United States of America.

JOHN HENRY LEWIN  
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DOUGLAS B. MAGGS  
GRANT W. KELLEHER

Special Assistants to the Attorney General.

THURMAN ARNOLD  
Assistant Attorney General.

DAVID A. PINE  
Attorney of the United States  
in and for the District of Columbia.

#### RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company, entitled "Your Health," began Wednesday October 19 and will run consecutively for thirty-six weeks. The program is broadcast each Wednesday over the blue network of the National Broadcasting Company at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).<sup>1</sup>

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

January 4. Fool's Gold.  
January 11. Only a Cold!  
January 18. Scarlet Fever, Measles and Whooping Cough.

#### Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

#### CONNECTICUT

**Society News.**—A public meeting was held in Hartford November 7 by the Hartford Medical Society and the Hartford County Medical Association; Dr. Emil Novak, Baltimore, discussed "Cancer—A Message of Hope."—Dr. Gustaf E. Lindskog, New Haven, addressed the Torrington Medical Society on "Recent Advances in Chest Surgery" November 2.—The Waterbury Medical Association recently held its first public health forum. Drs. David R. Lyman, New Haven, Cole B. Gibson, Meriden, and James J. Hennessy, Hartford, discussed "Early Diagnosis of Tuberculosis, Especially in the 'Teen Age Group.'"—At a meeting of the Tolland County Medical Association in Somers in October Dr. Morton Arnold, Willimantic, spoke on "Treatment of Common Diseases of the Ear, Nose and Throat."—The Windham County Medical Association was addressed in Willimantic October 20 by Dr. Allan M. Butler, Boston, on subsidized medicine.

#### DISTRICT OF COLUMBIA

**The Blood Bank at Gallinger.**—The "blood bank" recently established at Gallinger Hospital, Washington, has proved to be successful and arrangements are now under way to expand it, newspapers report. About 80 pints of blood is being dispensed each month. After each transfusion the hospital requests friends or relatives of a patient receiving blood from the "bank" to donate blood to replenish the supply. Having a supply of various types of blood in the "bank" eliminates delays formerly encountered when in emergencies it was discovered that a patient needed an immediate transfusion. Under the new plans, the "blood bank" will be housed in three special rooms at the hospital, under the direction of a junior surgeon and a graduate nurse, to supervise all operations in the additions to the blood stock, its typing, preservation and maintenance of accurate records.

#### FLORIDA

**Society News.**—In accordance with a recently granted charter, the Dade County Medical Society will henceforth be known as the Dade County Medical Association, Inc. The old charter was dissolved.—At a recent meeting of the DeSoto-Hardee-Highlands County Medical Society, the name of the society was changed to DeSoto-Hardee-Highlands-Charlotte-Glades County Medical Society.—The Duval County Medical

1. Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.

Society was addressed recently by Drs. John Webster Merritt on "Hyperthyroidism from a Medical Viewpoint" and Frank G. Slaughter, "Complications in Thyroid Surgery."—A clinic at the Duval County Hospital was a feature of the ninth annual meeting of the Florida Society of Dermatology and Syphilology, November 20.

**Public Health Meeting.**—The tenth annual meeting of the Florida Public Health Association was held at the Hollywood Beach Hotel, Hollywood, November 28-30. The speakers included:

- Dr. William H. Spiers, Orlando, Public Health from the Standpoint of the Practicing Physician.
- Dr. James N. Patterson, Jacksonville, Evaluation of the More Common Serodiagnostic Tests for Syphilis.
- Dr. George N. MacDonell, Miami, Possibility of the Introduction by Means of Airplane Travel of Yellow Fever into the United States.
- J. J. Taylor, Tallahassee, The New Food, Drug and Cosmetic Act and Its Public Health Aspects.
- Dr. Leon Banov, Charleston, S. C., Practicable Public Health.

## ILLINOIS

**Society News.**—At a meeting of the Sangamon County Medical Society in Springfield December 1 the speakers were Drs. Ralph A. Kinsella and James L. Mudd, both of St. Louis, on "The Pneumonia Situation" and "Surgical Treatment of Bronchiectasis" respectively.—Dr. Charles K. Petter, Waukegan, discussed "Surgical Treatment of Pulmonary Tuberculosis" before the Rock Island County Medical Society at the county tuberculosis sanatorium December 13.

## Chicago

**Dr. Fishbein to Address Public Meeting.**—Dr. Morris Fishbein, Editor of THE JOURNAL, will address a public meeting at the Chicago Woman's Club January 4 under the auspices of the Chicago Medical Society. His subject will be "Don't Be Your Own Doctor."

**Personal.**—Dr. Lloyd L. Arnold, professor of bacteriology and public health at the University of Illinois College of Medicine and director of the Chicago laboratories of the state department of health, has been appointed a member of the city board of health, succeeding Dr. Louis E. Schmidt, resigned. Dr. Schmidt's duties as secretary of the board will be taken over by Dr. Francis A. Dulak, a member since 1934.

## KANSAS

**New District Society.**—The Twelfth Councilor District Medical Society was organized at a meeting in Garden City October 30 with the following officers: Drs. Grant R. Hastings, Lakin, president, Herman C. Sartorius, secretary, and George O. Speirs, Spearville, councilor. Eighteen counties comprise the district. It is planned to hold three meetings each year, rotating between Dodge City, Garden City and Liberal.

**Graduate Course on Obstetrics and Pediatrics.**—A graduate course on obstetrics and pediatrics opened November 28 in Norton under the auspices of the state board of health in cooperation with its committee on maternal and child welfare and financed with social security funds. The course will also be given in Colby, Garden City, Liberal and Dodge City for four consecutive weeks. The instructors are Drs. Morris Edward Davis and William J. Dieckmann, department of obstetrics and gynecology, University of Chicago, and Rollin E. Cutts and John M. Adams, department of pediatrics, University of Minnesota.

## LOUISIANA

**Personal.**—The New Orleans Eye, Ear, Nose and Throat Society gave a dinner in honor of Dr. Otto Joachim November 11 to commemorate his seventy-fifth birthday and the fiftieth anniversary in the practice of medicine in New Orleans.

**District Meetings.**—Dr. Emmett L. Irwin, New Orleans, addressed the Second District Medical Society in New Orleans October 20 on diseases of the abdomen.—At a meeting of the Fourth District Medical Society in Shreveport October 4 the speakers were Drs. John H. Musser and Arthur Neal Owens, both of New Orleans, on "Modern Serum Therapy of Pneumonia" and "The Operative Reconstruction of Facial Defects" respectively.

## MAINE

**Society News.**—Dr. Raymond V. N. Bliss, Blue Hill, read a paper before the Androscoggin County Medical Society in Auburn November 17 entitled "Hospitals and Laity Take Up the Practice of Medicine in Ruritania."—The Portland Medical Club was addressed November 1 by Dr. Oscar R. Johnson

on syphilis.—At a meeting of the Kennebec County Medical Association in Waterville November 17 Dr. Harold Edward MacMahon, Boston, spoke on Bright's disease.—Dr. Frederick T. Lord, Boston, discussed "Pneumococcus Pneumonia" before the Penobscot County Medical Association in Bangor November 15.—Dr. Henry C. Knowlton, Bangor, addressed the Piscataquis County Medical Association November 17 on diabetes.—At a meeting of the Sagadahoc County Medical Society recently Dr. Willard H. Bunker, Calais, spoke on current medical problems confronting the profession at the present time.—Dr. Charles D. Cromwell, Fairfield, discussed tuberculosis before the Somerset County Medical Society in Solon recently.—Dr. Maxwell E. Macdonald, Boston, discussed "Emotions and Bodily Changes" before the Cumberland County Medical Society December 9.

## MICHIGAN

**Joint Tuberculosis Meeting.**—A joint meeting of the Michigan Tuberculosis Association, Michigan Trudeau Society and Michigan Sanatorium Association was addressed October 15 by the following speakers, among others:

- Dr. Lauren F. Busby, Northville, A Study of Basilar Lesions in Pulmonary Tuberculosis.
- Drs. William M. Tuttle, Detroit; Christopher J. Stringer, Lansing, and Edward J. O'Brien, Detroit, Studies on the Sputum of Tuberculous Patients Treated by Extrapleural Thoracoplasty.
- Dr. Anthony D. Calomeni Jr., Saginaw, Fate of the Contralateral Lung in Pulmonary Tuberculosis.

**Child Guidance Clinic.**—A grant of \$11,000 from the Children's Fund of Michigan, Detroit, will be used to launch a program of state subsidized child guidance clinics throughout Michigan, newspapers reported. The first clinic will be established in Lansing to serve Ingham, Eaton and Clinton counties and it is expected that a second will be started in Saginaw within a year. The staff of the first unit will be composed of a psychiatrist, a psychologist and psychiatric social agents. The local government will supply quarters and clerical and stenographic help and the professional staff will be furnished by the state, assisted by the grant from the Children's Fund. Dr. Joseph E. Barrett, state hospital director, will supervise the program.

## NEW HAMPSHIRE

**Fiftieth Anniversary Celebration.**—Dr. Henry O. Smith, Hudson, was honored by citizens of the town November 10 with a dinner celebrating his fiftieth anniversary of practice there. More than 200 attended and addresses were made by town officials and by Dr. Frank E. Kittredge, Nashua. Dr. Smith received a watch as a memento.

**State Tuberculosis Meeting.**—The annual meeting of the New Hampshire Tuberculosis Association was held in Manchester October 6. Dr. Clifford E. Waller of the U. S. Public Health Service, Washington, D. C., was the principal speaker, on "The State Program for Control of Tuberculosis."

## NEW JERSEY

**New Executive of State Society.**—Dr. Norman M. Scott, lieutenant colonel, U. S. Army, retired, has been appointed executive assistant of the Medical Society of the State of New Jersey to work with Dr. Leroy A. Wilkes, Trenton, executive officer, in carrying on the administrative work of the society.

**District Meetings.**—A meeting of the Third District Branch of the Medical Society of New Jersey was held in Princeton November 17. The speakers were Drs. Hilton S. Read, Atlantic City, on "Medicine a Social Service"; William J. Carrington, Atlantic City, "What Changes in Medical Practice in 1939?"; Albert G. Hulett, East Orange, "Medical Preparedness," and David McCabe, Ph.D., Princeton, "Economics in Relation to Medicine."

**County Society Banquet.**—The Gloucester County Medical Society held its annual banquet October 20 at the Pitman Country Club. Dr. Wilmer Krusen, president of the Philadelphia College of Pharmacy and Science, Philadelphia, was the guest speaker, on "Medicine Yesterday, Today and Tomorrow." Dr. Hilton S. Read, Atlantic City, showed motion pictures of a trip to Greece and Dr. Frank Overton, Trenton, editor of the *Journal of the Medical Society of New Jersey*, discussed a medical history of New Jersey, for which data are being collected. Dr. Elwood E. Downs, Woodbury, received the society's medal of honor for his contributions as poet laureate of the physicians of Gloucester County.

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MAJOR



**Surgical Society Meeting.**—Dr. Alfred L. Hathcock, Palestine, was elected president of the Texas Surgical Society at its annual meeting in Galveston October 10-11. Drs. William L. Crosthwait, Waco, and Eutus P. Bunkley, Stamford, were elected vice presidents and Dr. Richard J. White, Fort Worth, was reelected secretary. Dr. Gershom J. Thompson, Rochester, Minn., was the guest speaker on "Treatment of the Enlarged Prostate."

#### VIRGINIA

**Regional Meetings.**—The Fourth District Medical Society met in Farmville November 22 with the following speakers, among others, Drs. John Powell Williams, Richmond, "General Medical Applications of Sulfanilamide"; Goldsborough Foad McGinnes, Richmond, "Proper Care of Diphtheria and Scarlet Fever," and Herbert C. Jones and Wilbur Allen Parker, Petersburg, "Regional Ileitis."—The Southside Virginia Medical Association held its quarterly meeting December 13 in Petersburg. The speakers included Drs. Hyman Cantor, Petersburg, on "Treatment of Chronic Ulcer of the Leg"; Harry J. Warthen Jr., Richmond, "Strictures of the Rectum, Benign and Malignant," and Douglas G. Chapman, Richmond, "The Heart Beat Mechanism in Health and Disease."—At a meeting of the South Piedmont Medical Society in Halifax November 22 the speakers were Drs. Hugh H. Trout, Roanoke, on "Posthospital Care of Surgical Patients"; Kinloch Nelson, Richmond, "Diagnosis and Treatment of Aortic Syphilis," and Frederick C. Rinker, Norfolk, "Treatment of Constipation."

#### WASHINGTON

**Women's Clubs Sponsor Health Meeting.**—The Seattle Federation of Women's Clubs conducted a three day health meeting in October. The first day was devoted to discussion of syphilis, with Drs. Donald G. Evans, state health officer, Glenn S. Usher and Stephen T. Parker as speakers. On the second day Drs. Delbert H. Nickson, Donald V. Trueblood and Frederick A. Slyfield spoke on cancer and on the third the subject was maternal and child hygiene, with papers by Drs. Gordon G. Thompson, Frederick B. Joy and Percy F. Guy.

#### PHILIPPINE ISLANDS

**Society News.**—At a meeting of the Manila Medical Society August 9 Dr. Jose C. Locsin, Silay, president of the Philippine Islands Medical Association, was the guest of honor and the speakers were Drs. Vicente F. Delfin, Manila, on "Autohemotherapy in Glaucoma," and Paterno S. Chikiamco, Manila, "X-Ray Diagnosis in Pulmonary Tuberculosis" respectively.

**National Research Council Meeting.**—At the twenty-third scientific conference of the National Research Council August 12 the speakers were Drs. José J. Vergara and Florencio Z. Cruz, on "Epidemiology of Ileocolitis and Dysentery"; Alfredo Pio de Roda, "Bacteriology of Ileocolitis Among School Children," and Benjamin Barrera, "Bacteriology and Pathology of Ileocolitis in Children." All are from Manila.

#### GENERAL

**Committee on Asphyxia Neonatorum.**—A committee of women physicians and registered nurses has been formed as a subcommittee of the Society for the Prevention of Asphyxial Death with the aim of awakening interest in the problem of asphyxia neonatorum. The committee is urging the establishment of a department of pneumatology in every hospital to direct the use of gases for the control of pain, for resuscitation and for treatment of disease. It is also seeking to enroll expectant mothers as members. Physicians and others interested are invited to communicate with Dr. Antoinette Perillo, acting chairman, 42 East Seventy-Eighth Street, New York.

**Grants of the Ella Sachs Plotz Foundation.**—Grants for research on problems of medicine and surgery are available from the Ella Sachs Plotz Foundation, according to an announcement. The maximum size of grants will usually be less than \$500. There are no formal application blanks, but letters asking for aid must state definitely the qualifications of the investigator, an accurate description of the proposed research, the amount requested and the specific use of the money to be expended. Letters should be in the hands of the executive committee before April 1939. During the past year thirty-two grants were made, sixteen to scientists outside the United States. Applications should be sent to Dr. Joseph C. Aub, Collis P. Huntington Memorial Hospital, 695 Huntington Avenue, Boston.

## Foreign Letters

### LONDON

(From Our Regular Correspondent)

Dec. 4, 1938.

#### Psychiatric Sequels of Head Injuries

At a meeting of the Royal Medico-Psychological Society Dr. S. A. MacKeith read a paper on the minor psychiatric sequels of head injuries. The official figures of the great war have led both British and foreign observers to dismiss as insignificant the influence of trauma in producing minor psychoses and psychoneuroses, but Mapother has doubted this conclusion. The minor post-traumatic psychiatric syndromes ranged from the "fright neurosis," described by Kraepelin, to the condition known as traumatic encephalopathy, which was the commonest of the syndromes. Less suitable names which had been applied to the latter were traumatic psychasthenia, post-traumatic dementia and the postconcussion syndrome. The main symptoms were headache, dizziness, intolerance to alcohol and inordinate fatigue on effort. Though there were often no neurologic signs, it was now generally agreed that the condition was of organic origin. A blow on any part of the head could produce it; its strength was not important. It was not necessary for the skull to have been fractured, nor was retrograde amnesia or history of unconsciousness essential. The symptoms were increased by excitement, exertion, bending down and changes in the weather. Variability in their intensity was characteristic. Sometimes headache was replaced by a "dazed feeling in the head."

The pathologic change in traumatic encephalopathy was a disturbance of intracranial equilibrium, probably due to a combination of factors, of which the chief was a continuously irritable cerebral circulation. In most cases a complete neurologic examination would reveal a few physical signs. When the diagnosis was doubtful, vestibular function and auditory acuity should be tested. The visual fields should be carefully examined and notice taken of any visual symptoms. Encephalograms, manometric examination of the spinal fluid and biochemical examination of the cerebrospinal fluid were also important, and the psychiatric examination should be thorough. Typical symptoms included impairment of judgment and loss of interest, initiative and power of adaptation.

Widely different pathologic changes had been reported: diffuse pinpoint hemorrhages, alterations in ganglion cells, necrosis of the walls of the smaller blood vessels, glial proliferation, and ependymal and subependymal lesions. There was no general agreement about the prognosis. In some cases ability to work was never recovered. With regard to this the question of whether the patient's job involved much mental work was important. In the treatment rest was indicated. Writers had reported relief of the headache by lumbar puncture, trephining and encephalographic examination.

#### A National Cancer Service

The government has announced its intention to establish a cancer service, which will make available for every one the modern facilities for the diagnosis and treatment of cancer. The mortality from cancer has been steadily rising for many years and the annual number of deaths from the disease in England and Wales is now 70,000. It is computed that not more than one in every four patients with cancer at an accessible site, and less than that in whom the disease is deep seated, is given an opportunity for the cure or amelioration offered by the prompt application of modern methods. According to the minister of health "There are vast resources of knowledge in our laboratories which are not yet carried through to the lives of the people."



### A New International Standard for Vitamin B

The first international standard for vitamin B, which consisted of an adsorbate of the antineuritic vitamin, made from rice polishings, on fullers' earth, has been replaced by crystalline vitamin B hydrochloride. This has been made possible by the synthetic preparation of the vitamin in pure crystalline form. The international unit is defined as the antineuritic activity of 3 micrograms of the international standard preparation and has been adopted by the permanent commission on biologic standardization of the Health Organization of the League of Nations. Like other international vitamin standards, the new standard is held on behalf of the League of Nations at the National Institute of Medical Research in England and is sent from there to national control centers established in other countries for distribution to laboratories and research workers.

### The Prophylaxis of Tetanus

All ranks of the British army are undergoing inoculation with tetanus toxoid, which is believed to confer a life-long immunity from tetanus. The process of inoculation has been proceeding for several months and it is hoped to complete it by the end of the year. Two injections are given at an interval of several weeks, and immunity is believed to be complete soon after the second one. The inconvenience caused by the inoculations is so slight that they have been done during the height of the training season. During the great war there was a serious mortality from tetanus. The aim has been to evolve a much more effective method of prevention than was then used.

### PARIS

(From Our Regular Correspondent)

Dec. 3, 1938.

### French Medical Association Meeting

This year's meeting of the French Medical Association was held at Marseilles November 10-12. The subjects chosen for special reports and general discussion were (1) the hypochloremias, (2) icterohemorrhagic spirochetosis (infection jaundice) and (3) the treatment of avitaminosis in adults.

#### THE HYPOCHLOREMIAS

A paper on the pathologic changes in chlorine deficiency was presented by Professor Ambard of Strasbourg and his co-workers. The chloropenia syndrome can be the result of (a) a decrease in the chlorine content of the blood plasma, (b) a diminution in the quantity of chlorides in the tissue or (c) a combination of the two. It is observed with acidosis, high intestinal obstruction, adrenal insufficiency and a few other clinical conditions. The administration of chlorides has a remarkably favorable influence. As to the cause, the loss of chlorine is considered in France to play the most important part. Some authors believe that either dehydration or the loss of sodium is the vital factor. Recently there has been a tendency to believe that it is impossible to distinguish the role of each of these three factors because they all take part in giving rise to the syndrome. It is of the utmost importance to agree on what is the normal amount of sodium chloride in the blood plasma. In a normal person, with a diet containing 10 or 12 Gm. of sodium chloride in twenty-four hours, the normal amount of chlorine in the blood plasma is from 0.36 to 0.365 mg. per hundred cubic centimeters, which may drop to 0.2 mg. when there is hypochloremia. It is indispensable in order to appreciate the significance of the chlorine content of the plasma to know the degree of intracellular and extracellular dehydration. In general the drug in the chlorine content of the plasma is a good index of the degree of chloropenia. Clinically the interpretation of the chloropenia syndrome is complicated. The clinical manifestations are not proportional to the drop in the chlorine content of the plasma. They

are related more particularly to the drop in sodium content; hence the plasma content of both electrolytes, chlorine and sodium, must be kept in mind in the analysis of the chloropenia syndrome.

The second paper, on the medical aspects of hypochloremia, was read by Dr. René S. Mach of Geneva, who suggested classifying the disease according to two principal types, (a) hypochloremia with dechloridization, as observed with excessive vomiting, severe diarrhea, profuse perspiration, diabetic coma and Addison's disease, and (b) hypochloremia without dechloridization. The latter is the result of a loss of equilibrium between the chlorine content of the blood and of the body tissues, as observed during pneumonia, certain types of nephritis, in association with severe burns and after operations. In certain cases the two types merge into so-called mixed hypochloremia.

The third paper, on the surgical aspects of hypochloremia, was read by Dr. Yves Bourde of Marseilles, who concluded (1) that the administration of chlorides is indicated in most surgical cases in which there is an incipient or definitely established toxic syndrome, (2) that both before and during such treatment, frequent chemical examinations of the blood should be made, (3) that a high degree of nonprotein nitrogen retention in the blood is not a contraindication to the administration of sodium chloride and (4) that when the chlorine content of the blood plasma is found to be definitely below normal the administration of sodium chloride is always indicated but that hyperchloremia is, on the other hand, a contraindication.

#### INFECTIOUS JAUNDICE

The epidemiology and the icteric forms of spirochetosis were the subject of the first paper, by Drs. Jules Monges and Jean Olmer of Marseilles.

The common form is infectious icterus with febrile recurrences. The average incubation period is five days for infection by the digestive route and fifteen days for infection by the cutaneous route. At the onset the fever is of four or five days' duration, but with an unfavorable prognosis it may last only twenty-four hours. The chief symptoms at this stage are severe headache and myalgia with a predilection for the muscles of the calf and the neck. In about 20 per cent of the cases a herpes on the lip or, occasionally, elsewhere is noted. The icterus appears on the fourth or fifth day, when the fever recedes. In most cases the stools are acholic. Splenomegaly and hepatomegaly are always found. As to renal symptoms, examination of the urine reveals albumin, red blood cells and casts. As a rule there is a marked rise in the nonprotein nitrogen content of the blood. Meningeal symptoms are often present, with slight changes in the spinal fluid. Striking features at the height of the disease are bleeding from the nose and gums and discrete purpura. The apyrexia lasts from four to seven days and is followed as a rule by the recurrence of a high temperature on the fifteenth to twentieth day. This relapse, or second febrile period, varies in duration from two to eight days.

In the severe form, which is rarely seen in France, the onset resembles that of the common form but the meningeal symptoms are more marked. A striking feature is the sudden drop in temperature on the fifth or sixth day. The icterus may appear as early as the second or third day and is very intense. Renal involvement is more severe than in the common form. Oliguria, with from 100 to 150 cc. in twenty-four hours, albuminuria and the presence of casts are accompanied by a rise in the nonprotein nitrogen content of the blood to from 600 to 900 mg. per hundred cubic centimeters. Hemorrhages are more often present and more severe than in the common form. Death usually occurs between the seventh and twelfth days, rarely later from uremia. Recovery is rare, only a few cases having been observed.

Benign infectious icterus is a third form, and with apparently catarrhal icterus, certain atypical symptoms should lead the clinician to think of a spirochetic origin. Symptoms seldom observed with ordinary catarrhal icterus, such as severe myalgia and arthralgia, herpes, a high temperature, marked icterus, signs of meningeal irritation, albuminuria, casts and a high nonprotein nitrogen content in the blood, should lead to a search for spirochetosis.

The mortality of infectious icterus is high in Japan, from 30 to 48 per cent, but much lower in France, where the less severe form has been observed. The most reliable method of diagnosis is examination of the blood serum for the typical reaction. Treatment has been chiefly symptomatic. Sero-therapy, as suggested by Pettit and Martin, has been employed but little in France, a few favorable results having been reported.

Leptospirosis without icterus was the subject of a paper by Profs. Jean Troisier and Maurice Bariéty of Paris. The term leptospirosis is based on the work of Noguchi and is being more frequently employed than spirochetosis. There are three distinct forms, the meningeal, the renal and the purely febrile. The first is a syndrome greatly resembling meningitis, accompanied by herpes in 27 per cent of the cases, a high temperature and an increased number of leukocytes in the spinal fluid. One of the characteristic features is the relapse, or recurrence of all the symptoms, which occurs as a rule between the fourteenth and twenty-third days. The average duration of the relapse is eight or nine days.

The existence of a renal form is not generally accepted. In some cases the clinical picture is that of nephritis with a high temperature. Further study is required before one can speak of a purely febrile leptospirosis.

## BERLIN

(From Our Regular Correspondent)

Nov. 22, 1938.

### Types of Diphtheria Bacilli

Dr. Preuner of the institute of hygiene at Göttingen University discussed the types of diphtheria bacilli before the Göttingen Medical Society. He pointed out that the attempt to fight diphtheria epidemics with isolation and mass examinations of bacillus carriers had not met with success. Despite these activities, severe epidemics have continued to recur. So many culture smears have been collected by the public examination centers that bacteriologic diagnosis has tended to become a routine study, whereas to be of maximal value a diagnostic examination must be based on the peculiarities of the individual case. The additional danger exists that certain persons may be classified as bacillus carriers because their throats harbor certain pathogenic micro-organisms although these in no way resemble diphtheria bacilli. Type diagnosis of the bacillus should always be established. It is not enough to determine the principal pathogenic types, *Typus gravis*, *Typus intermedius* and *Typus mitis*; other frequently present organisms, such as the paradiaphtherial, diphtheroid and pseudodiphtherial, should be looked for. Also it is demonstrable that in culture smears of material from the throats of sick persons the pathogenic diphtheria bacilli change to diphtheroid or pseudodiphtheria bacilli. Conversely, however, one has not as yet been able to observe the phenomenon experimentally, although to do so seems theoretically plausible.

### DISSIMILAR IMPORTANCE OF THE THREE TYPES

Dr. Preuner went on to point out the dissimilar value of the three pathogenic types with regard to epidemiology. For example, in the Königsberg epidemic of 1935-1936, *Typus intermedius* participated to a relatively greater extent than *Typus gravis*; furthermore, the pathogenicity of the former has greatly increased in recent times. The problem of the differing patho-

genicity of the three types has become a prominent topic of discussion chiefly in the last few years. Recent examinations of 4,200 smears demonstrated that virtually an equal number of mild illnesses were caused by each of the three principal types. This observation substantiates the objection formerly advanced by clinicians, namely that the prognosis need be no more unfavorable in the presence of *Typus gravis* than in the presence of *Typus mitis*. However, the investigations revealed that only 8 per cent of all persons infected with *Typus gravis* and some 10 per cent of all infected with *Typus intermedius* were bacillus carriers, whereas the corresponding proportion of *Typus mitis* carriers was 25 per cent. The same differences were noted in cases of moderately severe involvement and in fatal cases. This suggests a certain diversity in the pathogenicity of the types. According to Doull's recent computations, the probability of infection is from six to twelve times greater for a person in the vicinity of a diphtheria patient than for a person in the vicinity of a carrier of diphtheria bacilli and around 120 times greater than for a completely unendangered person. It should be kept in mind that the foregoing figures are based chiefly on the observation of patients and persons in the vicinity of patients, and by this means, to be sure, only a small proportion of bacilli are detected. Since, however, every fourth person infected with *Typus mitis* is already a bacillus carrier, the relative harmlessness of the carriers of this type is demonstrated. Mention must be made of the great clinical importance of mixed infections with different types of diphtheria bacilli. Such infections were represented by 15 per cent of all the examination material. Transformation of one type into another is improbable, since of the patients treated at home only 8 per cent and of the patients treated in hospitals 22 per cent had mixed infections. Moreover, in 200 cases a deterioration was manifested if a primary infection with *Typus mitis* was followed by an infection with *Typus gravis* or *Typus intermedius*.

Dr. Preuner arrives at the conclusion that the police health regulations and the useless mass examinations for diphtheria ought to be curtailed. On the contrary, he would make obligatory at all examination centers diagnosis of the exact type of diphtheria bacillus. Patients infected with *Typus gravis* should in particular be protected against subsequent infection with the other types. He felt, however, that the measure which would hold the most promise of real success would be the absolutely inclusive, active protective inoculation against diphtheria of all children under 14.

## BELGIUM

(From Our Regular Correspondent)

Nov. 19, 1938.

### Reeducation of Convalescents from Tuberculosis

In recent years many studies have been made of the precarious period during which the tuberculous patient passes from sanatorium care to the resumption of occupational activity. It is agreed that a stage of supervised transition is necessary, and this period should if possible be so organized as to reeducate the convalescent in an occupation.

With these purposes in view the Station-école de rééducation et d'apprentissage was founded as a unit of the Marcinelle Sanatorium. The station school consists of two sections, the apprenticeship section and the reeducation section. Assignment of a convalescent to one of the sections is made by the medical director, who takes into account not only the physical capacity of the patient but also his erstwhile occupation and the occupation which he hopes to follow after leaving the sanatorium. The normal working day totals seven hours and is divided into periods from 8 to 10 a. m., 10:15 a. m. to 12:15 p. m. and 1:30 to 4:30 p. m. The pupils are gradually placed on a full time schedule. During an introductory period they spend two hours in the workshop each day; the period is increased later

to four hours and finally to seven hours. This progression is supervised by the medical director, who decides the length of each convalescent's working day on the basis of weekly examinations. As a rule convalescents on a seven hour schedule receive remuneration on the basis of output, quality and rate of speed at which work is done. The funds to pay their wages are obtained from the sale of their handiwork. Strict medical supervision appears to be indispensable, and the convalescents understand that it is to their advantage that they be required to work. They realize the importance of this period of reeducation, they know that the work represents a supplementary treatment and they wish wholeheartedly to "undergo" the occupational therapy.

The part played by the sanatorium's social aid service reinforces the results obtained in the school. Each convalescent who has participated in the work is obliged to report to the social aid two months or less before leaving the sanatorium. Guided by suggestions, he seeks a job by applying to former employers or organizations which might employ him after his period of reeducation.

The social aid service takes all necessary steps in this regard; it functions through the authority properly vested in it as well as through the outside cooperation of the "Help the Tuberculous" society.

### The Blood in Benzene Poisoning

Dr. F. Mignolet reported to the Société médico-chirurgicale de Liège a study of twenty-six cases of benzene poisoning. Speaking from the hematologic point of view, the author called attention to the following facts: 1. The alarm signal of a hemopathy based on benzene poisoning is thrombopenia with prolongation of the coagulation time. 2. Granulopenia is in itself a clear sign of poisoning. 3. The anemias accompanying severe intoxication are of the aplastic hyperchromic type in a majority of cases. 4. Eosinophilia is relative and not absolute. 5. The bleeding times are prolonged but diminish as the hemogram returns to normal.

## Marriages

HAROLD A. TAGGERT, Drexel Hill, Pa., to Mrs. Anita Ancill Mendenhall of Upper Darby, New York, October 8.

FRANK JOSEPH CURRAN, New York, to Miss Charlotte Eugenia Conway at Laurel Cliff, Va., October 1.

GUSTAVE NERI CLICK, Pensacola, Fla., to Miss Adelaide Woodhouse West in Norfolk, Va., October 5.

JAMES SCOTT TEMPLETON, Pinckneyville, Ill., to Miss Elizabeth Boheim of Du Quoin, September 1.

JEAN L. CAPTAIN, Montclair, N. J., to George Burr Sabine, Ph.D., of Rochester, N. Y., October 8.

BONNELLE W. RHAMY to Miss Elma Louise Miller, both of Fort Wayne, Ind., October 19.

WILLIAM TAYLOR CUMMINS to Mrs. Laura E. Gruss, both of San Francisco, September 28.

CLAYTON E. BUHL, Nebraska City, Neb., to Miss Anne Frehling of Haigler, October 1.

EDWARD C. VOGES, Terre Haute, Ind., to Miss Lois L. Walker of Clinton, October 16.

DUANE W. CRANKSHAW, Hatteras, N. C., to Miss Agnes Tolson of Buxton, October 12.

ARTHUR B. CECIL, Los Angeles, to Miss Henrietta Smith at Yuma, Ariz., recently.

HERMAN CHOR, Chicago, to Mrs. Suzanne Noble in Lake Bluff, Ill., December 10.

OTTO C. CHRISTMANN to Mrs. Elizabeth Broughton, both of Seattle, September 2.

DAVID ALLEN HERSTEIN to Miss Ruth Smith, both of Chicago, December 11.

L. PAUL HART to Miss Ruth Lensing, both of Evansville, Ind., October 4.

EDGAR ROGGE to Miss Celeste Firnstahl, both of Seattle, September 9.

## Deaths

Lionel Louis Cazenavette ☉ New Orleans; Medical Department of Tulane University of Louisiana, New Orleans 1897; professor of clinical neurology at his alma mater; formerly professor of diseases of the nervous system at the Graduate School of Medicine of Tulane University; member of the American Psychiatric Association; at one time connected with the U. S. Public Health Service; medical superintendent of the City Hospital; aged 64; died, October 15.

Theodor Teimer ☉ Newark, N. J.; Medizinische Fakultät der Universität Wien, Austria, 1897; formerly member of the city board of health; served in various capacities at the Newark City Hospital, Presbyterian Hospital, Beth Israel Hospital, Newark Eye and Ear Infirmary, St. Mary's Hospital, Orange and Essex County Hospital, Belleville; aged 66; died, October 12, of coronary thrombosis.

Robert Leslie Carson, Rochester, N. Y.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1890; on the staffs of the Rochester General and Rochester State hospitals and of the Frederick Fern Thompson Hospital, Canandaigua, N. Y.; aged 74; died, October 10, of epithelioma of the ear with metastases, and cerebral arteriosclerosis.

Sidney Capers Zemp, Camden, S. C.; University of Pennsylvania Department of Medicine, Philadelphia, 1896; member of the South Carolina Medical Association; served during the World War; formerly on the staff of the Camden Hospital; aged 70; died, October 14, in the Veterans Administration Facility, Atlanta, Ga.

James Anderson Crockett, Stanberry, Mo.; University of Missouri School of Medicine, Columbia, 1903; member of the Missouri State Medical Association; county coroner; for many years president of the board of public works of Stanberry; president of the Gentry County Medical Society; aged 62; died, October 28.

Holman Bernard, Pilot Mountain, N. C.; Medical College of Virginia, Richmond, 1912; member of the Medical Society of the State of North Carolina; served during the World War; formerly member of the state legislature; aged 49; died, October 25, in the Martin Memorial Hospital, Mount Airy, of pneumonia.

Andrew Jackson Cauthen, Lancaster, S. C.; Medical College of the State of South Carolina, Charleston, 1930; member of the South Carolina Medical Association; formerly health officer of Lancaster and Chesterfield counties; aged 36; was killed, October 31, in an automobile accident.

Henry McIlree Williamson Gray, Montreal, Que., Canada; University of Aberdeen Faculty of Medicine, Scotland, 1895; F.R.C.S., Edinburgh, 1902; served during the World War; aged 68; on the staff of St. Mary's Hospital, where he died, October 6, of heart disease.

John B. Wadlington, Princeton, Ky.; Southwestern Homeopathic Medical College and Hospital, Louisville, 1899; member of the Kentucky State Medical Association; formerly county health officer; aged 62; died, October 3, of pneumonia and heart disease.

James Martin Graham, Asheville, N. C.; Atlanta School of Medicine, 1912; formerly connected with the Veterans Administration; served during the World War; aged 52; died, October 7, of injuries received when he fell from the roof of his home.

Adelbert J. McIntyre, Seattle; University of Oregon Medical School, Portland, 1897; at one time mayor and member of the school board of Hoquiam, Wash.; aged 67; died, October 26, of cerebral thrombosis and bronchopneumonia.

Charles Baum, Middletown, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1877; for many years president of the board of trustees of the Gettysburg College; aged 83; died, October 26, of coronary occlusion.

William Elsworth Allen ☉ Rock Island, Ill.; Chicago College of Medicine and Surgery, 1910; served during the World War; on the staff of St. Anthony's Hospital; aged 50; died, October 28, in Chicago of cerebral hemorrhage.

Joseph Albert Waska ☉ Chicago; Bennett College of Eclectic Medicine and Surgery, Chicago, 1905; member of the staff of the Evangelical Deaconess Hospital; aged 65; died, October 28, of carcinoma of the intestine.

William Wesley Gill, Madison, Wis.; Rush Medical College, Chicago, 1883; medical director and vice president of the

National Guardian Life Insurance Company; aged 78; died, October 3, of cerebral hemorrhage.

**Jerry E. Vanderpool**, Walla Walla, Wash.; Kansas Medical College, Topeka, 1896; formerly health officer; aged 72; was found dead, October 29, near Bellingham, of carbon monoxide poisoning, self administered.

**Alson R. Gilbert**, Elwood, Ill.; Northwestern University Medical School, Chicago, 1901; member of the Illinois State Medical Society; aged 64; died, October 21, in St. Joseph's Hospital, Joliet, of heart disease.

**John Edward Wesley Anderson**, Scotland, Ont., Canada; Trinity Medical College, Toronto, 1884, and L.R.C.P., Edinburgh, Scotland, 1884; aged 76; died, October 25, as the result of being scalded with hot water.

**William Lee Miller**, Bemis, W. Va.; University of Maryland School of Medicine, Baltimore, 1894; member of the West Virginia State Medical Association; aged 73; died, October 12, of arteriosclerotic heart disease.

**Edwin Anderson Tufts** Ⓢ Arkansas City, Kan.; National University of Arts and Sciences Medical Department, St. Louis, 1915; on the staff of the Mercy Hospital; aged 58; died, October 4, of pneumonia.

**Francis Xavier Shea**, Everett, Mass.; Harvard University Medical School, Boston, 1921; member of the Massachusetts Medical Society; aged 44; died, October 2, of coronary occlusion and asthma.

**Elmer E. Waller**, Springcreek, Tenn. (licensed in Tennessee in 1908); member of the Tennessee State Medical Association; aged 59; died, October 19, of arteriosclerosis, hypertension and myocarditis.

**Harriet Caroline Beringer Alexander**, Chicago; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1883; aged 79; died, October 12, of arteriosclerosis.

**Louis P. Treiber**, Escanaba, Mich.; Illinois Medical College, Chicago, 1904; member of the Michigan State Medical Society; aged 61; died, October 22, of coronary occlusion.

**Warren Buckland Beach**, Delphos, Kan.; Kansas Medical College, Medical Department of Washburn College, Topeka, 1900; aged 65; died, October 12, of coronary thrombosis.

**Golston D. Bingham**, Sugar Grove, N. C.; University of Tennessee Medical Department, Nashville, 1905; aged 66; died, October 7, of acute dilatation of the heart.

**Harriet Otella Funk Given**, McCordsville, Ind.; Central College of Physicians and Surgeons, Indianapolis, 1901; aged 68; died, October 30, of cerebral hemorrhage.

**Joseph Lowry Baird** Ⓢ Marked Tree, Ark.; College of Physicians and Surgeons, Memphis, Tenn., 1910; aged 55; died, October 31, of cerebral hemorrhage.

**John Watson**, Minneapolis; Bellevue Hospital Medical College, New York, 1874; aged 90; died, October 4, in the Northwestern Hospital of bronchopneumonia.

**Fred Millard Adams**, Decatur, Ill.; Northwestern University Medical School, Chicago, 1901; aged 65; died, October 27, of hypostatic pneumonia.

**Clara I. Darr**, Portland, Ore.; Homeopathic Hospital College, Cleveland, 1889; aged 81; died, October 7, in Pittsburgh of carcinoma of the sigmoid.

**Jesse Moody Oliver**, Hazlehurst, Ga.; Atlanta School of Medicine, 1910; aged 51; died, October 18, of acute biliary cirrhosis of the liver.

**James Clough Dorr**, Dansville, N. Y.; University of Buffalo School of Medicine, 1896; aged 70; died, October 28, of arteriosclerosis.

**Albert F. Padberg**, Canton, Okla.; St. Louis College of Physicians and Surgeons, 1909; aged 63; died, October 12, of heart disease.

**Elmer Ellsworth Garrett**, Troy, Iowa; Chicago Medical College, 1889; aged 78; died, October 15, of cerebral hemorrhage.

**Edwin M. Land**, Marengo, Ind.; Hospital College of Medicine, Louisville, Ky., 1904; aged 60; died in October of miliary tuberculosis.

**Gerrit John Warnshuis**, Detroit; Detroit College of Medicine, 1916; aged 45; was killed, October 27, in an automobile accident.

**Forde Morgan**, New York; Bellevue Hospital Medical College, New York, 1892; aged 70; died, October 8, of heart disease.

**James H. Colby**, Purcell, Okla.; Missouri Medical College, St. Louis, 1890; aged 71; died, October 12, of cerebral hemorrhage.

## Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

### INTELLIGENCE TESTS

*To the Editor:*—Please give advice concerning methods of "intelligence rating" which might be applicable to adults in a mental institution. Where might I obtain the materials for such a test? M.D., Texas.

**ANSWER.**—Intelligence tests may be divided into two general types—verbal and nonverbal. The verbal tests require and assume an average acquaintance with the English language, while the nonverbal tests do not require such ability. Of the verbal tests the most widely used is the Stanford revision of the Binet-Simon test. This is applicable to persons from the ages of 3 through 18. The army alpha tests are valuable and consist of a group of tests wherein the following abilities are measured: following directions, arithmetical problems, common sense, synonym-antonym, correction of disarranged sentences, number series completion, analysis and information.

The nonverbal performance tests are especially useful when examining persons who speak only a foreign language or children with speech, reading or hearing handicaps. The Pintner-Paterson test, the Kohs block design and Porteus maze scale, the Goodenough "drawing a man" test and the Healy picture completion tests are often valuable for measuring the intelligence of adults.

All "intelligence tests" should be viewed as psychologic or psychometric hurdles and are helpful in evaluating the general ability of a patient. However, it must be borne in mind that lack of attention, emotional depression or obsessive preoccupation can distract the patient from focusing on these tests and thereby give erroneous results concerning the evaluation of intelligence.

### References:

Terman, L. M., and Merrell, M. A.: *Measuring Intelligence*, New York, Houghton Mifflin Company, 1937.

Terman, L. M.: *Condensed Guide for the Stanford Revision of the Binet Simon Intelligence Tests*, New York, Houghton Mifflin Company, 1920.

Pintner, R. A., and Paterson, D. C.: *A Scale of Performance Tests*, New York, D. Appleton & Co., 1917.

Reichard, J. D.: *Intelligence of the Prospective Immigrant*, Pub. Health Bull. 206, July 1933.

Materials and tests may be purchased from C. H. Stoelting Company, 424 North Homan Avenue, Chicago.

### LOCAL MEDICATION FOR RHINOPHARYNGITIS

*To the Editor:*—Please outline a desirable technic for the use of a pressure spray apparatus in office nose and throat treatments of rhinopharyngitis and other similar respiratory infections. The method I am following at present is one-third strength hexylresorcinol spray, 5 per cent mercurochrome swabbing and a menthol scented vapor. Please include reference to recent literature.

M.D., Washington, D. C.

**ANSWER.**—Acute rhinitis and acute nasopharyngitis not only have local manifestations but are frequently accompanied by constitutional symptoms. The most logical treatment would be rest in bed, plenty of fluids and citrus fruit juices, soft diet and salicylates.

The pathologic condition in the nose and pharynx may be merely localized manifestations of a general infection. Furthermore, it is widely believed that these infections are self limited and that topical applications do not cut short the course of the illness in any way, although some measure of relief may be obtained by way of applications to the nose and pharynx.

The studies of the physiology of the nasal mucosa as revealed by the work of Proetz (*Ann. Otol., Rhin. & Laryng.* 43:450 [June] 1934), Stark, Lierle, Moore, Hilding and Walsh and Cannon (*ibid.* 47:579 [Sept.] 1938) now allows intranasal medication which is based on more scientific reasons than color, strength and smell. They have shown particularly that the popular concept that "at least it is something harmless to do" is a dangerous one. Aqueous solutions of drugs used experimentally in the nose in rabbits have entered the lungs, causing inflammation and necrosis. Oily solutions probably do not come into contact with the nasal mucosa at all, lying as

they do on the mucous blanket and interfering with ciliary streaming. When used indiscriminately, especially in debilitated infants, their role in the causation of lipid pneumonia is not theoretical. Such antiseptics as merthiolate 1:1,000 and mercurochrome 2 per cent produce slowing of the cilia. Furthermore, from the work of Archibald, Brown, Cannon and Walsh it is doubtful whether antiseptics, in the strength used or the time in contact, can exert any significant bacteriostatic or bactericidal effect.

The maintenance of the physiologic functioning of the nasal mucous membrane and the promotion of adequate drainage from the nasal sinuses are the two essentials in the treatment of upper respiratory infections. Therefore, for office treatment, pledgets moistened with weak saline solutions of ephedrine hydrochloride 0.5 to 1 per cent or neosynephrine hydrochloride 0.25 to 0.5 per cent appear to be the medications of choice for intranasal application.

#### AMYOTROPHIC LATERAL SCLEROSIS.

*To the Editor:*—I have a case of amyotrophic lateral sclerosis. There is no question about the diagnosis. The patient had iron, quinine and strychnine, quinine, aminoacetic acid, vitamin B and prostigmine. I would appreciate your opinion regarding the treatment. Are there any new useful therapeutic means and drugs for treating such a case?

M.D., Michigan.

**ANSWER.**—Amyotrophic lateral sclerosis is incurable and invariably fatal. It is the most common cause of true bulbar palsy and because of that is likely to produce death by asphyxiation and choking. There is no specific treatment. Potassium iodide in doses of 1 Gm. (15 grains) three times daily may be used. Strychnine sulfate in doses of from 0.0010 to 0.0016 Gm. (one-sixtieth to one-fortieth grain) three times daily may be tried. Prostigmine, aminoacetic acid, jello and ephedrine have not produced any significant help in the management of these cases. If there is any evidence of a syphilitic infection the patient must receive vigorous antisyphilitic therapy. The patient should get good food and much rest. If he is unable to swallow, tube feeding must be resorted to.

#### EXAGGERATED MOTILITY OF PENIS

*To the Editor:*—A man aged 35, whom I have had under observation for two years, complains of exaggerated motility of the penis. There is a downward motion (extension) followed immediately by a return to the original position. Sometimes the penis moves alone; at other times there is a retraction of the testes (cremasteric reflex) alone, and at times the two reactions occur together. The condition is more noticeable when sitting than when standing. He gives a history of excessive sexual activity accompanied by ingestion of alcohol at the time of intercourse for a period of about ten months during 1934. During 1935 and 1936 he was moved by his firm to another locality and engaged in sexual activity only sporadically, although he continued to indulge in alcohol. In 1937 he returned to his original location and after moderate sexual activity noticed the beginning of his trouble. There is no history of masturbation or venereal disease. He is an intelligent person and the underlying functional pathologic condition was explained to him. A regimen of regular sexual indulgence was outlined and the use of alcohol, coffee and tobacco was eliminated. There has been some improvement but not the complete cessation of motility that had been expected. He himself notices that when he consumes large quantities of fluids and urinates regularly the condition is not so noticeable. Likewise the wearing of more loosely fitting clothes has helped somewhat. He is resigned to getting along with the handicap but says that at times the motility distracts his attention, particularly during conversation. He notices also that when he is under tension the motility is aggravated. Results of a thorough physical examination were negative. The prostate is normal in size and microscopic examination of expressed secretion gives negative results. The Wassermann reaction is negative. Urologic consultants have not been able to offer anything of value except to agree that the condition is purely functional and might clear up spontaneously after a time. I would appreciate advice concerning the possibility of relief by means of surgery directed to the cremaster muscles or any other suggestions you might offer. He does not require the use of sedatives. How would you explain anatomically the functional pathologic condition involved?

M.D., Louisiana.

**ANSWER.**—It must be definitely established that the patient has no organic disease of the central nervous system, especially of the spinal cord. Has he had a complete examination of the nervous system and of the spinal fluid? If there is no objective evidence of organic disease the patient has in all probability a functional disorder. It is not uncommon for normal persons to have retraction of the testes and scrotum during increased emotional tension. The movements of the penis may be a form of masturbation. Surgery directed to the cremaster muscles will not effect a change. The only organic explanation that can be offered is that the movement of the penis is either an irritative phenomenon of the lumbosacral cord or a cortical release movement from a basal ganglion lesion (encephalitis). Similar move-

ments of the abdominal wall, lower and upper extremities, face and head have been known to occur in chronic lethargic encephalitis. The following suggestions are made:

Complete neurologic and spinal fluid examination; complete abstinence from alcohol; a mild sedative (sodium bromide 10 to 15 grains [0.65 to 1 Gm.] three times a day); copious amounts of fluid; exercises in the form of mild games and walks; at least eight to nine hours of sleep daily, with the patient lying on either side but not on the back, and encouragement that the condition will clear up in time. He should be informed, if it is true, that there is no organic disease and that he must learn to relax. All fears and erroneous ideas relative to his condition must be explained.

#### BURNS FROM NITROUS OXIDE

*To the Editor:*—A patient who works in a factory where nitrous oxide gas is made has asked me whether these workers are in any danger from the processes of manufacture. He recently burned his finger with ammonium nitrate. He did not come into the office until quite a deep wound had developed. Please inform me as to the proper immediate and subsequent treatment of such a burn.

MARTHA S. COTTELL, M.D., Novi, Mich.

**ANSWER.**—Nitrous oxide is usually prepared by heating ammonium nitrate in a retort at a temperature of 170-260 C. This causes the ammonium nitrate to decompose into nitrous oxide and water. At such a temperature this salt may inflict serious burns which are due not solely to heat but in part to chemical action. Rapid oxidation of tissues takes place, so that such burns are likely to heal slowly and to be accompanied by extensive scar formation.

Fresh burns should be subjected to wet dressings with mild alkalis or weak acids that act as alkalis in the presence of stronger acid substances. In the present instance wet dressings with sodium bicarbonate, boric acid or citrates might prove advantageous, followed, after a few hours, by the usual treatment for burns. Under some circumstances connected with the manufacture of nitrous oxide, nitrogen peroxide might be formed, which is dangerous and exposure may lead to pulmonary edema. This nitrogen peroxide, if present as an impurity, is commonly removed by scrubbing the gas mixture with an alkali solution, such as sodium carbonate. Here again some opportunity theoretically exists for the causation of a dermatitis as the result of the action of the sodium carbonate or of some other alkali.

#### TRANSMISSION OF COMMUNICABLE DISEASES BY BOOKS

*To the Editor:*—Is it possible for one to become infected with any of the communicable or contagious diseases through the use of books or magazines that have been used by persons so infected and returned to public or rental libraries or second-hand bookstores? I am interested mainly in colds, tuberculosis, typhoid and scarlet fever. Do the libraries or book stores use any method to sterilize the books before another customer receives them? Has the printer's ink any antiseptic or inhibitory action on viruses or bacteria? Is there any satisfactory method of sterilizing books without injury to the book or telltale odor? Has any one ever tried taking and growing cultures of pathogenic bacteria from books just returned to the library and those that have been on the shelves a few weeks?

M.D., Indiana.

**ANSWER.**—Communicable diseases are transmitted mainly by person rather than by inanimate objects. Books that have been handled recently by patients suffering from smallpox, scarlet fever or diphtheria may transmit such infections to susceptible persons. Usually board of health regulations would require such books to be destroyed. There is scant likelihood that common colds, tuberculosis or typhoid would be transmitted by library books or magazines. In most instances pathogenic organisms that might contaminate books soon cease to live outside the body.

Ordinarily libraries and book stores make no attempt to disinfect books that have been returned by customers. It is not likely that printer's ink has any antiseptic or inhibitory action on viruses or bacteria. Any viruses or bacteria present on books soon die in most cases because of the absence of moisture, heat and nutrient mediums for their existence.

Some years ago it was customary that books on premises under quarantine should be disinfected at the termination of quarantine by means of fumes of formaldehyde. Under such conditions the books were removed from the shelves or book-cases, opened and stood on end, being subjected to the fumes of formaldehyde for a period of from eight to twelve hours in a sealed room. At present it is generally believed that the exposure of books to sunlight and fresh air is equally effective. In most contagious disease hospitals books that are used by a

patient are generally destroyed when the patient leaves the hospital. In any event the patient is not allowed to take the books with him from the premises.

The *Illinois Health Messenger* (10:105 [Sept. 15] 1938) reported that Dr. Arthur H. Bryan of Baltimore City College made laboratory tests on books recently used by students and found few germs of any kind; those present were mostly of a harmless variety. Notwithstanding this report, books should be kept at a distance from the face, and the hands of the reader should not be brought constantly in contact with the mouth while the book is being read. The hands are one of the commonest agencies in transmitting infections. Consequently when a book is read the hands should be clean.

#### BLISTERS AND FURUNCLES

*To the Editor.*—Recently I saw a blister caused by friction on the heel which had been treated by the application of solutions of silver nitrate and tannic acid. The results seemed good. Can you give me the details of this method of treatment? What is considered the best method of treating blisters caused by friction on the hands and feet? What is the best ointment or other application for a furuncle to hasten suppuration? I have seen farmers in the South apply a slab of salty bacon rind to a boil at night with highly satisfactory results within from twelve to fifteen hours. I have never been able to produce equal results with any ointment or other local application.

A. C. SMITH, M.D., Bremerton, Wash.

*ANSWER.*—The use of solutions of tannic acid and silver nitrate for dressing eroded blisters is an extension of their employment for burns. For the latter, some surgeons remove what debris comes away quickly and easily and paint the parts with a 5 per cent aqueous solution of tannic acid. When this dries, it is followed with a 10 per cent solution of silver nitrate. Any method which protects eroded bullae from ordinary infection and pressure is useful. The latter is achieved by an agent which provides an impervious coating. A 2 per cent aqueous solution of gentian violet is efficient, or a covering with flexible collodion in which is incorporated an antiseptic may be used. Some antiseptic may be painted on the lesion and over that the collodion may be used.

Such beneficial action as salted bacon has in hastening the pointing of furuncles is achieved probably by virtue of its hypertonicity. Undoubtedly, a hypertonic salt solution in the form of a wet dressing would do as well. Hot wet dressings are probably superior to ointments as applications for furuncles. Many dermatologists find roentgen rays useful in the treatment of furuncles that have not yet pointed.

#### POSSIBLE POISONING FROM CERASAN

*To the Editor.*—I wish to inquire concerning a product used in treating seed wheat known as "cerasan," manufactured by du Pont of Wilmington, Del., as to its toxicology and the likelihood of one working in its dust becoming poisoned. A man aged 20 first came in contact with the dust of "cerasan" in April 1937, shortly after which he complained of malaise, lack of the usual strength and feeling of well being, persistent coryza and postnasal drip, which was diagnosed by an otolaryngologist as a chronic sinusitis due to the dust of "cerasan." After the seeding season was past he improved and by the fall of 1937 felt almost his normal self again. He began treating grain last spring in April and shortly after the same symptoms again were noted. I first saw him August 24, at which time he complained of fever, malaise and stiffness of all the joints of the body. The patient was well developed. His skin was rather flushed. The temperature was 102.2 F., the pulse rate 76 and the respiratory rate 22. There were moderately diminished breath sounds in the left midaxilla about the fifth to the sixth rib. The red blood cells numbered 4,500,000, the white blood cells 16,000. The urine was essentially normal. The Wassermann and Widal tests gave negative results. August 29 he developed severe pain in the left part of the chest just outside the border of the area of cardiac dullness and synchronous with respiration. After a day or two this subsided and a pericardial rub was noted together with formation of fluid in both of the pleural cavities. This was aspirated and of straw color, containing many polymorphonuclear leukocytes and a gram-positive streptococcus together with a gram-negative bacillus. By the first of September a distinct diastolic murmur was added to the existing systolic murmur and the friction rub disappeared. At present he is making progress toward recovery. I have diagnosed the case as being a bronchopneumonia with pleural effusion and pericarditis, but in view of the history of possible poisoning and the compensation which would thus be involved I am seeking information and if possible the experience of others with this toxic agent.

VIRGIAL PARRETT, M.D., Beach, N. D.

*ANSWER.*—"Cerasan" is believed to represent a mixture of 5 per cent ethyl mercury phosphate with 95 per cent inert material. It is ordinarily used in the proportion of one-half ounce to the bushel of grain. During the mixing of this material, farmers customarily tie a cloth over the nose and mouth. Among grain elevator workers where larger quantities are mixed, respirators are sometimes furnished and worn for pro-

tection against the possibility of mercury poisoning. Records of severe mercury poisoning from this compound as used in mixing and application are not known, but minor injuries probably arise and are chiefly manifested by edema of the glottis or larynx, possibly associated with ptialism. In the instance described the symptoms and signs are scarcely characteristic of mercury poisoning. Some of the classic features of mercury poisoning are salivation, gingivitis, inflamed buccal membranes, oral ulceration, gastrointestinal disturbance and malaise. In sub-acute poisoning systemic disturbances may follow or be superimposed on the acute manifestations just mentioned. Tremors arise, particularly in connection with voluntary movements. In severe chronic poisoning marked tremors and spasms appear which may involve the entire body. In chronic poisoning weakness may exist and cachexia may be present. If the manifestations mentioned in the query are compared with those later listed as typical of mercury poisoning, no great similarity appears to exist. The coryza, weakness and malaise are suggestive, but these conditions, which developed months after exposure, are scarcely the result of mercury poisoning. It is reasonable to believe that a minor mercury poisoning may have existed on both the occasions of handling "cerasan," but doubt may be entertained that the more severe manifestation that appeared months later is the direct result of this earlier exposure. However, if the patient's condition is of occupational origin, mercury probably is the cause and he should be examined carefully with regard to manifestations of mercury poisoning.

#### BACTERIA IN WATER USED FOR VENTILATION

*To the Editor.*—I want to get some information on the bacterial content of water used in ventilating and air conditioning systems. If such water is used over and over again, does it become heavily loaded with bacteria and does the air circulated from such a system become increasingly polluted? Is there any need for the use of germicides in such water? Are there any studies which have discussed these questions? If the water used to cleanse the air is changed often enough, there of course would be no problem, but as I understand it this is not true in some instances. Chemicals are used occasionally to keep down the growth of algae and to avoid corrosion of metals. Anything that you can refer me to on this subject will be appreciated.

W. A. SAWYER, M.D., Rochester, N. Y.

*ANSWER.*—The problem of bacteria in the air is one that has been undergoing rapid evolution in recent years. When polluted water is used for purposes of humidification, large numbers of bacteria may enter the air. The problem of the use of germicides in water used for air conditioning should be approached with great caution because of the toxic effects on man which these germicides may possess. Ultraviolet irradiation is at present being extensively studied as a means of purifying air.

#### References:

- Effect of Polluted Waters for Purposes of Humidification, Annual Report, Department of Public Health, Commonwealth of Massachusetts, Public Document 34, 1934, p. 166.
- Wells, W. F., and Wells, Mildred W.: Measurement of Sanitary Ventilation, *Am. J. Pub. Health* 28: 343 (March) 1938.

#### LINOTYPE OPERATOR AND TUBERCULOSIS

*To the Editor.*—A man aged 26 showed signs of pulmonary tuberculosis five months ago. He has been employed as a linotype operator for ten years. His occupation exposes him to lead, type and inks. Is there any special occupational hazard in this work which would make him more likely to acquire this disease? I would appreciate any references which would elucidate this point.

IRVING L. LYNN, M.D., Jersey City, N. J.

*ANSWER.*—It is well known that the pulmonary tuberculosis rate among those in the printing trades has been high; it was a great deal higher a few years ago than it is at the present time.

It has been suggested by various observers that possibly there is some relation between exposure to lead and tuberculosis. In spite of the fact, however, that there has been a wealth of clinical material and that the matter has been under consideration for many years, no one has definitely shown that there is any relation between the lead used in the trade and tuberculosis. Formerly a great many of the print shops were small and insanitary and a large percentage of the printers were alcoholic addicts.

In a recent publication by the National Tuberculosis Association the medical and legal aspects of tuberculosis as an occupational disease were discussed elaborately by Mary Graham Mack. In this pamphlet a large number of cases of tuberculosis in which there was claimed to be some relation between the disease and occupation are listed. There is no case listed in which the claimant was an employee of a printing establishment.

A discussion may be found in Chapter 11 of the 1925 edition of Alice Hamilton's "Industrial Poisons in the United States" (New York, Macmillan Company, 1925).



## Council on Medical Education and Hospitals

### ADDITIONAL HOSPITALS APPROVED

The Council on Medical Education and Hospitals of the American Medical Association has given its approval to the following hospitals since the publication of the last previous list in THE JOURNAL, July 23, 1938:

#### Hospitals Approved for Intern Training

Crawford W. Long Memorial Hospital, Atlanta, Ga.  
Methodist Hospital of Central Illinois, Peoria, Ill.  
St. Anthony's Hospital, Rockford, Ill.  
Methodist Episcopal Hospital, Gary, Ind.  
Parkside Hospital (col.), Detroit.  
City and County Hospital, Fort Worth, Texas.  
Luther Hospital, Eau Claire, Wis.

#### Hospitals Approved for Residencies in Specialties

Los Angeles County Hospital, Los Angeles.  
Anesthesia, Neurosurgery.  
St. Vincent's Hospital, Los Angeles.  
Radiology.  
White Memorial Hospital, Los Angeles.  
Anesthesia, Orthopedics, Urology.  
Alameda County Hospital, Oakland, Calif.  
Pathology.  
Olive View Sanatorium, Olive View, Calif.  
Thoracic Surgery.  
Hospital for Children, San Francisco.  
Gynecology, Orthopedics.  
St. Joseph's Hospital, San Francisco.  
Mixed.  
San Francisco Hospital, San Francisco.  
Ophthalmology.  
Stanford University Hospitals, San Francisco.  
Anesthesia, Pathology.  
Fairmont Hospital of Alameda County, San Leandro, Calif.  
Medicine.  
St. Mary Hospital, Pueblo, Colo.  
Mixed.  
Homeopathic Hospital, Wilmington, Del.  
Surgery.  
Duval County Hospital, Jacksonville, Fla.  
Medicine, Surgery.  
James M. Jackson Memorial Hospital, Miami, Fla.  
Medicine, Surgery.  
Norwegian-American Hospital, Chicago.  
Medicine, Surgery.  
Provident Hospital (col.), Chicago.  
Ophthalmology-Otolaryngology, Radiology.  
Ravenswood Hospital, Chicago.  
Obstetrics.  
Evanston Hospital, Evanston, Ill.  
Radiology.  
University Hospitals, Iowa City.  
Dermatology-Syphilology.  
Franklin Square Hospital, Baltimore.  
Surgery.  
Hospital for Women, Baltimore.  
Medicine, Surgery.  
Boston City Hospital, Boston.  
Anesthesia.  
University Hospital, Ann Arbor, Mich.  
Orthopedics.  
City of Detroit Receiving Hospital, Detroit.  
Psychiatry.  
Woman's Hospital, Detroit.  
Medicine.  
University Hospitals, Minneapolis.  
Anesthesia, Urology.  
Northern Pacific Beneficial Association Hospital, St. Paul.  
Mixed.  
St. Peter State Hospital, St. Peter, Minn.  
Psychiatry.  
Children's Mercy Hospital, Kansas City, Mo.  
K... .. Mo.  
Surgery, Urology.  
St. Luke's Hospital, Kansas City, Mo.  
Orthopedics, Pathology.  
Creighton Memorial St. Joseph's Hospital, Omaha.  
Medicine, Obstetrics-Gynecology, Pathology, Surgery.  
New Hampshire State Hospital, Concord, N. H.  
Psychiatry.  
New Jersey State Hospital, Marlboro, N. J.  
Psychiatry.  
Anthony N. Brady Maternity Home, Albany, N. Y.  
Obstetrics.  
Kings County Hospital, Brooklyn.  
Thoracic Surgery.  
Buffalo General Hospital, Buffalo.  
Orthopedics.  
Meadowbrook Hospital, Hempstead, N. Y.  
Malignant Diseases, Medicine.  
Hermann M. Biggs Memorial Hospital, Ithaca, N. Y.  
Tuberculosis.  
Middletown State Homeopathic Hospital, Middletown, N. Y.  
Psychiatry.  
Central and Neurological Hospital, New York City.  
Ophthalmology.

Harlem Hospital, New York City.  
Surgery.  
Lincoln Hospital, New York City.  
Anesthesia.  
Morrisania City Hospital, New York City.  
Traumatic Surgery.  
Mount Sinai Hospital, New York City.  
Orthopedics.  
New York Infirmary for Women and Children, New York City.  
Medicine, Obstetrics, Surgery.  
New York Post-Graduate Medical School and Hospital, New York City.  
Anesthesia.  
Roosevelt Hospital, New York City.  
Otolaryngology, Urology.  
Rochester General Hospital, Rochester, N. Y.  
Ophthalmology-Otolaryngology.  
Trinity Hospital, Minot, N. D.  
Medicine, Surgery.  
Christ Hospital, Cincinnati.  
Medicine, Surgery.  
Glenville Hospital, Cleveland.  
Mixed.  
Starling-Loving University Hospital, Columbus, Ohio.  
Ophthalmology-Otolaryngology, Pathology.  
Lucas County General Hospital, Toledo, Ohio.  
Medicine, Obstetrics-Gynecology, Surgery.  
Youngstown Hospital, Youngstown, Ohio.  
Medicine.  
Reconstruction Hospital and McBride Clinic, Oklahoma City.  
Orthopedics.  
Pittsburgh City Home and Hospitals, Mayview, Pa.  
Pathology.  
American Oncologic Hospital, Philadelphia.  
Malignant Diseases.  
Germantown Dispensary and Hospital, Philadelphia.  
Pathology.  
Hahnemann Hospital, Philadelphia.  
Medicine, Obstetrics-Gynecology, Surgery.  
Jefferson Medical College Hospital, Philadelphia.  
Medicine, Otolaryngology, Radiology, Surgery.  
P... .. Foundation, Pittsburgh.

G... .. of Meharry Medical College (col.),  
... .. Pediatrics, Surgery.  
... .. Tenn.  
... .. Pathology.  
John Sealy Hospital, Galveston, Texas.  
Pediatrics.  
Woodmen of the World War Memorial Hospital, San Antonio, Texas.  
Tuberculosis.  
Columbia Hospital, Milwaukee.  
Pathology.  
Milwaukee Children's Hospital, Milwaukee.  
Surgery.  
St. Joseph's Hospital, Milwaukee.  
Pathology.

## Medical Examinations and Licensure

### COMING EXAMINATIONS

#### STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, December 24, page 2416.

#### NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Medical centers having five or more candidates desiring to take the examination, Feb. 13-15, May 1-2 (Part II only—limited to a few centers), June 19-21, and Sept. 11-13. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th Street, Philadelphia.

#### SPECIAL BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: An Affiliate of the American Board of Surgery. Written examination, Part I, will be held in various cities of the United States and Canada, April 8. Oral examinations for all candidates, St. Louis, May 13-14. Applications must be filed not later than sixty days prior to the date of the examinations. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF INTERNAL MEDICINE: Written examinations will be held in various parts of the United States, Feb. 20. Application must be received on or before Jan. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: General oral, clinical and pathological examinations for all candidates, Part II examinations, (Groups A and B) will be held in St. Louis, May 15-16. Application for admission to Group A examinations must be on file in the Secretary's office by March 15. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: Written. March 15 (applications must be filed not later than Feb. 15) and Aug. 5. Oral. St. Louis, May 15 and Chicago, Oct. 6. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Memphis, Tenn., Jan. 13-14. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: St. Louis, May 12-13 and Chicago, Oct. 6-7. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PATHOLOGY: Richmond, Va., April 8-9. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: St. Louis, May 16. Appointments must be made before Jan. 16. Cincinnati, Nov. 14-15. Appointments must be made before July 14. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF RADIOLOGY: St. Louis, May 11-14. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: New York, Jan. 13-15. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

## Michigan June Examination at Ann Arbor

Dr. J. Earl McIntyre, secretary, Michigan State Board of Registration in Medicine, reports the examination held at Ann Arbor, June 14-15, 1938. One hundred and fifteen candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists.....		(1938) 82.4,†	86.3
University of California Medical School.....		(1938) 87.2,*	87.7*
Georgetown University School of Medicine.....		(1933)	86.8
Emory University School of Medicine.....		(1937)	85.8
Northwestern University Medical School.....		(1938) 85.6,*	88.2
Rush Medical College.....		(1937)	83.8
School of Medicine of the Division of Biological Sciences.....		(1937) 83.8,†	85,†
Harvard University Medical School.....		(1935)	87.8,†
(1936) 86.4,† 87.3			
University of Michigan Medical School.....		(1936)	86.3,†
(1938) 80.1,† 80.1,† 80.6,† 80.9,† 81.1,† 81.7,† 81.7,† 82.1,† 82.2,† 82.6,† 83.1,† 83.2,† 83.2,† 83.4,† 83.4,† 83.6,† 83.6,† 83.6,† 83.6,† 83.8,† 83.9,† 84,† 84.1,† 84.2,† 84.3,† 84.3,† 84.3,† 84.4,† 84.4,† 84.4,† 84.5,† 84.5,† 84.5,† 84.6,† 84.7,† 84.7,† 84.7,† 84.8,† 84.8,† 84.8,† 85.1,† 85.1,† 85.2,† 85.2,† 85.2,† 85.2,† 85.3,† 85.4,† 85.4,† 85.4,† 85.4,† 85.5,† 85.5,† 85.5,† 85.5,† 85.6,† 85.7,† 85.8,† 85.8,† 85.8,† 85.9,† 86,† 86,† 86,† 86.1,† 86.1,† 86.1,† 86.1,† 86.3,† 86.3,† 86.3,† 86.3,† 86.4,† 86.4,† 86.5,† 86.5,† 86.6,† 86.6,† 86.7,† 86.7,† 86.8,† 87.4,† 87.5,† 87.5,† 87.7,† 87.7,† 87.7,† 87.8,† 87.9,† 87.9,† 89.2,† 90.2,†			
Columbia University College of Physicians and Surgeons.....		(1937) 84.2, (1938)	86.3†
University of Pennsylvania School of Medicine.....		(1937)	85.4,
(1938) 87.9†			
Marquette University School of Medicine.....		(1938)	81.8.*
82.9,* 84.6, 86,* 86.9*			

\* This applicant has completed the medical course and will receive the M.D. degree on completion of internship. License has not been issued.  
† License has not been issued.

## Michigan June Examination at Detroit

Dr. J. Earl McIntyre, secretary, Michigan State Board of Registration in Medicine, reports the examination held at Detroit, June 14-15, 1938. Ninety candidates were examined, eighty-nine of whom passed and one failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists.....	(1938)		86.9
Georgetown University School of Medicine.....	(1937) 84.4,		85.1
Loyola University School of Medicine.....	(1937) 82.3, (1938)		84.7
Northwestern University Medical School.....	(1937)		85,
(1938) 82, 83.2, 83.6, 84,* 85			
University of Illinois College of Medicine.....	(1937)		86
Wayne University College of Medicine.....	(1937)		83.5,
(1938) 76.1,† 79.6,† 80.8, 80.9,† 81,† 81,† 71.4,† 81.4,† 81.8,† 81.8,† 81.9,† 81.9,† 82,† 82.1,† 82.1,† 82.3, 82.3,† 82.4,† 82.5,† 82.5,† 82.6,† 82.8,† 82.8,† 82.9,† 82.9,† 82.9,† 83,† 83,† 83,† 83,† 83.1, 83.1,† 83.1,† 83.3,† 83.4,† 83.7,† 83.8,† 83.9,† 84,† 84,† 84,† 84.1,† 84.1,† 84.1,† 84.1,† 84.1,† 84.2,† 84.3,† 84.7,† 84.8,† 84.9,† 84.9,† 85,† 85.1,† 85.2,† 85.3,† 85.3,† 85.4,† 85.4,† 85.5,† 85.7,† 85.7,† 85.8,† 85.9,† 85.9,† 86.1,† 86.3,† 86.6,† 86.7,† 86.7,† 86.8,† 86.9,† 87.1,† 87.2,† 87.3,†			
University of Minnesota Medical School.....	(1938)		86.3*
Washington University School of Medicine.....	(1936)		83.3*

School	FAILED	Year Grad.	Per Cent
National University of Athens School of Medicine.....	(1916)	67.7	

\* License has not been issued.  
† This applicant has received the M.B. degree and will receive the M.D. degree on completion of internship. License has not been issued.

## Washington July Report

Mr. Harry C. Huse, director, Department of Licenses, reports the written examination held at Seattle, July 18-20, 1938. The examination covered seven subjects and included seventy questions. An average of 70 per cent was required to pass. Fifty-nine candidates were examined, all of whom passed. Twenty-two physicians were licensed by reciprocity and twelve physicians were licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Arkansas School of Medicine.....	(1937) 73.5,	80.7	
College of Medical Evangelists.....	(1938) 78.7,	84	
University of Colorado School of Medicine.....	(1937)	84.1	
George Washington Univ ..		80	
Loyola University School ..		81.4,	
Northwestern University ..	(1938) 82.7, 83.1, 83.5, 86.7, 88.2, 90.1		
Rush Medical College.....	(1932)	84.8,	
(1936) 83.8, (1937) 79, 84, 84.1			
Indiana University School of Medicine.....	(1937) 82.2,	82.7	
Johns Hopkins University School of Medicine.....	(1932)	82	

Harvard University Medical School.....	(1934)	85.2,
88.5, (1937) 85, 86.7		
University of Michigan Medical School.....	(1933)	76.7
University of Minnesota Medical School.....	(1938)	87.7
St. Louis University School of Medicine.....	(1937) 80.2,	83.1
Washington University School ..	(1937)	79.1
Creighton University School ..		80.4, 80.5, 87.2
University of Nebraska College ..	(1928)	77,
(1932) 78.1, (1936) 77.7, (1937) 85.2		
Columbia University College of Physicians and Surgeons.....	(1937)	81.2,
87.1		
Western Reserve University School of Medicine.....	(1937)	85
University of Oregon Medical School.....	(1936)	81.5,
82.7, (1937) 78.5, 82, 82.2, 82.4, 82.5, 83, 85, 86.5, 91.5.		
Jefferson Medical College ..	(1925)	81
University of Pennsylvania ..	(1934)	89.4
Baylor University College ..	(1937)	78.8
McGill University Faculty of Medicine.....	(1936) 78.7, (1938)	78.4
University of Edinburgh Faculty of Medicine.....	(1926)	77.1

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Stanford University School of Medicine.....	(1935, 2)		California
University of Colorado School of Medicine.....	(1935)		Colorado
Rush Medical College.....	(1934)		California
School of Medicine of the Division of Biological Sciences.....	(1937)		California
State University of Iowa College of Medicine.....	(1928)		California,
(1928), (1937) Iowa			
Johns Hopkins University School of Medicine.....	(1934)		Maryland
University of Michigan Medical School.....	(1930)		California
University of Minnesota Medical School.....	(1934)		Montana
St. Louis University School of Medicine.....	(1934, 2)		Missouri
University of Nebraska College of Medicine.....	(1925),		
(1937) Nebraska, (1937) Oregon			
University of Oregon Medical School.....	(1937, 3)		Oregon
University of Virginia Department of Medicine.....	(1937, 2)		Virginia
McGill University Faculty of Medicine.....	(1937)		Oregon

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medi ..			B. M. Ex.
Yale University ..			B. M. Ex.
Johns Hopkins ..			B. M. Ex.
University of N ..			B. M. Ex.
University of C ..			B. M. Ex.
Jefferson Medic ..			B. M. Ex.
McGill Universi ..			B. M. Ex.

## Wyoming October Examination

Dr. G. M. Anderson, secretary, Wyoming State Board of Medical Examiners, reports the written examination held at Cheyenne, Oct. 3, 1938. The examination covered eleven subjects and included 110 questions. An average of 75 per cent was required to pass. Two candidates were examined, both of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Loyola University School of Medicine.....	(1938)	78	
University of Illinois College of Medicine.....	(1938)	86.7	

## Colorado October Examination

Dr. Harvey W. Snyder, secretary, Colorado State Board of Medical Examiners, reports the written examination held at Denver, Oct. 5-7, 1938. The examination covered eight subjects and included 163 questions. An average of 75 per cent was required to pass. Seven candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Colorado School of Medicine.....	(1937)	85	
Medizinische Fakultät der Universität Wien (1912) 80,			
(1921) 80, (1937) 76			
Osteopaths ..		80.5, 84, 84.5	
* Licensed to practice medicine and surgery.			

## Tennessee September Examination

Dr. H. W. Qualls, secretary, Tennessee State Board of Medical Examiners, reports the written examination held at Memphis, Sept. 28-29, 1938. The examination covered ten subjects and included 100 questions. An average of 75 per cent was required to pass. Twenty-five candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Arkansas School of Medicine.....	(1938)	86.7	
Howard University College of Medicine.....	(1934)	85	
Northwestern University Medical School.....	(1937)	83.8	
Tulane University of Louisiana School of Medicine.....	(1938) 85.7,	85.9	
St. Louis University School of ..		85.1, 87.3	
University of Tennessee College ..		83.8,	
85.2, 85.3, 85.5, 86.1, 86.2,			
86.8, 87, 87.5, 87.5, 87.6, 87.8			
University of Edinburgh Faculty of Medicine.....	(1921)	90.4	

## Book Notices

**Vitamin B<sub>1</sub> (Thiamin) and Its Use in Medicine.** By Robert R. Williams, Sc.D., and Tom D. Spies, M.D., Associate Professor of Medicine, University of Cincinnati. Cloth. Price, \$5. Pp. 411, with 20 illustrations. New York: Macmillan Company, 1938.

The growth promoting and antineuritic values of different foods, such as yeast and liver, originally were considered to be the properties of a single substance. Now it is known that the antineuritic substance is one factor, called vitamin B<sub>1</sub> or thiamin. The growth promoting value is due to several factors. Vitamin B<sub>1</sub> and three other substances are included in the heat labile fraction of the vitamin B complex. The heat stable fraction includes riboflavin, nicotinic acid, vitamin B<sub>6</sub> and several other substances which, unlike the preceding three, are not readily adsorbed from an aqueous solution. Throughout the present monograph the authors have carefully considered the relationship of vitamin B<sub>1</sub>, the subject of their study, to the other factors of the B complex, as far as they are known.

The antineuritic factor of foods was first clearly recognized by Eijkman in 1897. By 1915 investigations had proceeded to the point where it became generally accepted that Eijkman's factor is the substance the lack of which leads to beriberi in man and polyneuritis in the fowl. The substance was not isolated until 1926, when it was obtained by Jansen and Donath; the structure was determined by Williams in 1936, and synthesis was accomplished by Williams and Cline and by others in 1936 and 1937. Thus a period of approximately forty years elapsed between the original description of polyneuritis in the fowl, and its cure with rice polishings, and the final isolation and synthesis of vitamin B<sub>1</sub>. The crystalline substance is now known as thiamin chloride, a name proposed by Williams at the request of the Council on Pharmacy and Chemistry for a suitable descriptive name that would not be therapeutically suggestive.

Thiamin, or vitamin B<sub>1</sub>, is widely distributed in nature, and of all the vitamins it is the one most universally needed by all forms of life. It is needed for the growth of many plants and micro-organisms, some of which can synthesize it for their own use. It is needed by insects and, indeed, by all animals that have been tested. The chief function of thiamin is concerned with the metabolism of carbohydrates. The thiamin requirements of man are proportional to the carbohydrate content of the diet. In some animal species, such as the rat, the thiamin requirements can be made extremely low by elimination of the preformed carbohydrate from the diet.

The authors point out that vitamin B<sub>1</sub> deficiency in man is more common than has been generally recognized. They point out that therapy may well be directed along three lines, namely the elimination of conditions which may cause excessive requirements for vitamin B<sub>1</sub>, the administration of vitamin B<sub>1</sub> in adequate amounts to correct the deficiency, and suitable treatment of coexisting diseases. They conclude that thiamin chloride is useful in the treatment of many clinical entities associated with undernutrition and peripheral neuritis.

The book is divided into two parts. Approximately the first hundred pages comprises a concise account of the available information which is considered to be of immediate value in the practice of medicine. The second part of the book is a somewhat more detailed presentation of the historical and experimental evidence derived from laboratory work.

The volume bears witness to the accuracy of the statement in the foreword by J. S. McLester that "In no other area of medical knowledge has there been recorded such a far-reaching advance as has been made during the past two decades in the field of nutrition. Pointing the way to the development of a healthier, more vigorous race, this advance marks an epoch in man's progress."

This book is one of the series of medical monographs under the general editorship of George R. Minot. It would be well if similar monographs were made available of the biochemistry and clinical applications of each of the substances which, like vitamin B<sub>1</sub>, are essential in the diet.

**Martini's Principles and Practice of Physical Diagnosis.** Edited by Robert F. Loeb, M.D., Professor of Medicine, College of Physicians and Surgeons, Columbia University. From the Authorized Translation by George J. Farber, M.D., Assistant in Roentgenology, Johns Hopkins University School of Medicine. Second edition. Cloth. Price, \$2. Pp. 213, with 30 illustrations. Philadelphia, Montreal & London: J. B. Lippincott Company, 1938.

In this little book on physical diagnosis the author has attempted to combine simplicity with enough theory to make the material understandable and interesting. It is written especially for the medical student who is entering the subject for the first time. Thus, although all essentials are included, there is no attempt to be encyclopedic. The discussion of the physics of auscultation and percussion is especially thorough. The author, a student of Friedrich Mueller's, has contributed previously to the subject. The editor is a well known clinician and investigator. The presentation is excellent. There is more discussion and less listing than in most books on this subject. Because of this it proves rather interesting reading. In this edition changes have been made in the sections on the respiratory tract and the circulatory system, and emphasis has been placed on abnormalities in the venous pressure. The last two sections are particularly well done. Because it is a simple, concise and yet reasonably complete account of physical diagnosis, this book should especially prove satisfactory to the medical student just commencing the subject.

**Ergebnisse der Vitamin- und Hormonforschung.** Herausgegeben von L. Ruzicka und W. Stepp. Band I. Mit einem Vorwort von Sir Frederick Gowland Hopkins. Bearbeitet von W. Berblinger et al. Cloth. Price, 34 marks. Pp. 470, with 44 illustrations. Leipzig: Akademische Verlagsgesellschaft M. B. H., 1938.

Many advances are being made in our knowledge of the hormones and vitamins, and the publication of a periodic review of progress in these interrelated fields should be most useful. The first volume of the present review was published in September 1937. It contains a historical foreword by Sir Frederick Gowland Hopkins followed by six articles in German, four in English and one in French. The authors are E. Glanzmann, A. Giroud, R. L. Stehle, C. A. Elvehjem, H. von Euler, W. Berblinger, R. R. Williams, H. Guggisberg, T. Reichstein, M. W. Goldberg and G. F. Marrian. The topics include the chemistry of vitamin B<sub>1</sub> and the chemistry of the hormones of the posterior lobe of the pituitary gland, adrenal cortex extract and the sex hormones. The subjects of two other reviews are the biochemistry of several components of the vitamin B complex and the significance of chemical activators and related substances in cells. The remaining subjects are the importance of vitamins during childhood, the distribution of vitamin C in body tissues and fluids, the relationship between the sex glands and the hypophysis, and the vitamins in relation to reproduction. There is a complete index of names of authors mentioned in the text, but no subject index.

**The Story of the Lying-In Hospital of the City of New York.** By James A. Harrar, M.D., Attending Obstetrician and Gynecologist, The Lying-In Hospital. Cloth. Pp. 83, with illustrations. New York: The Society of the Lying-In Hospital, 1938.

This booklet traces the founding and development, administrative as well as medical, of the Lying-In Hospital of the City of New York. There was an epidemic of yellow fever in New York in 1798 and, to care for the wives rendered "wretched by grief and poverty," Dr. David Hosack proposed the foundation of a lying-in hospital, which was effected in 1799, the year George Washington died. The first venture failing of support, an arrangement was made with the New York Hospital for the use of a ward. The maternal mortality was 4 per cent, mostly from sepsis. In 1827 the liaison was broken and the institution enjoyed a paper existence until 1855, when a plan of paying part of poor women's obstetric expenses at home was adopted. The endowments of the Society of the Lying-In Hospital accumulated until 1890. In 1889 J. W. Markoe, Samuel Lambert, H. McM. Painter and J. Clifton Edgar had opened the "Midwifery Dispensary" in the lower east side of New York for the home care of poor women and the teaching of medical students. They were having financial troubles. They learned of and merged with the paper organization, but the paper was worth \$300,000. In 1890 J. Pierpont Morgan became interested when he heard the story of a

cesarean section done in the home by Dr. Markoe; he gave \$300 to provide comforts for the poor woman and later (1897) donated \$1,350,000 for the imposing building at Seventeenth Street and Second Avenue (opened in 1902). The home service continued to grow with the hospital development, and 69,071 consecutive tenement deliveries had been made in 1918 with an uncorrected mortality rate of 3.156 per thousand (a startling proof of the inherent safety of home obstetrics). The hospital was a pioneer in the relief of labor pain and evolved the Gwathmey technic. While much in the line of research was produced, the greater accomplishment was in clinical teaching. In the twenties, financial difficulties beset the vast institution and its annual deficit was more than J. P. Morgan Jr. could make up, wherefore the great financier got J. D. Rockefeller to give \$2,000,000, Mr. G. F. Baker & Son \$2,000,000 and he gave the same all within a few days just like that. The hospital now became the Maternity Department of the New York Hospital, associated with Cornell University Medical College. Prof. H. J. Stander became its head but the old staff was given a place in the new administration. A gynecologic department was established in the new hospital on the East River near Seventieth Street. The development of this institution reflects the changes going on in the world. The present happy relations between a full time and part time staff prove that such an arrangement is practicable.

**Physiology of the Nervous System.** By J. F. Fulton, M.A., D.Phil., M.D., Sterling Professor of Physiology, Yale University, New Haven, Conn. Cloth. Price, \$6. Pp. 675, with 95 illustrations. New York, Toronto & London: Oxford University Press, 1938.

Here is a great book concerning the functions of the nervous system, so well written that it is equally adapted for use by medical students, research workers or clinicians. Only the highest praise can be given this work. It is packed with facts and current concepts, well documented, bolstered by an extensive bibliography and easily available through an excellent subject and author index. The historical basis of each phase of neurophysiology introduces the chapters in which anatomy, physiology and suggestions for clinical application are integrated in a scholarly fashion rarely found in textbooks. A summary is appended to each chapter. Loreño de No prepared the chapter on the cyto-architecture of the cerebral cortex and nowhere else is a more authentic account to be found. Neurologists have long awaited such a work; the book should be used in all medical schools and carefully studied by all neurologists and neurophysiologists.

**A B C of the Vitamins: A Survey in Charts.** By Jennie Gregory, M.S. Foreword by Walter H. Eddy, Professor of Physiological Chemistry, Teachers College, Columbia University, New York. Cloth. Price, \$3. Pp. 93. Baltimore: Williams & Wilkins Company, 1938.

This book is a collection of charts and drawings about the vitamins. The publishers explain that, by the visual instruction method employed in this book, "long-winded definitions" are replaced by pictures, so that every one now can visualize difficult reading matter. Some of the illustrations are of interest, especially the maps of the world, which show in a greatly simplified form the geographic distribution of vitamin A deficiency, beriberi, scurvy, rickets and pellagra. But on the whole the material gives one the impression of being far removed from the laboratory, clinic or kitchen. Chemical structures can be written in books or on blackboards but they do not tell how a process is carried out in the laboratory. Simplified growth curves without ordinates or abscissas may illustrate the failure of guinea pigs to grow on a vitamin C deficient diet, but the curves obviously do not tell enough. The drawings are purposely made simple, but would it be a sign of mental deficiency to inquire why the tails of all the rats curve upward in the air, except for the big fellow shown sitting on top of a fence, whose tail is hanging down? The drawings are incomplete representations of the whole story; while they may be used to supplement a text, they hardly could be used satisfactorily to replace it. The book contains some charts which are too complex for the general reader and too simple for the person desiring complete information. An example is the illustration showing the relationship between blood calcium and inorganic phosphate, vitamin D and the parathyroids. The author has attempted in this chart to present the

mechanisms of rickets, tetany, hypervitaminosis D and osteitis fibrosa. Many of the terms provided in the glossary afford another example of material which is unnecessary for the general reader and inadequate for the student.

**The Form and Functions of the Central Nervous System: An Introduction to the Study of Nervous Diseases.** By Frederick Tilney, M.D., Ph.D., and Henry Alsop Riley, M.D., Director and Attending Neurologist, West Service, Neurological Institute, New York. Foreword by the late George S. Huntington, Sc.D., M.D. Third edition. Cloth. Price, \$10. Pp. 851, with 600 illustrations. New York: Paul B. Hoeber, Inc., 1938.

The third edition of this deservedly popular book on basic anatomic and physiologic data concerning the nervous system appears fifteen years after the preceding edition. The authors have modified much of the material to conform to the progress in the field but have maintained their individual and unusual form of presentation. Both authors have done extensive anatomic research, which explains the heavy anatomic loading of this tremendous tome. Profuse illustrations of gross and microscopic morphology dominate the book. For an anatomic orientation the book is highly recommended. The physiology is considerably weaker and in certain sections not down to date. The manner of clinical presentation artificially mechanizes localization and diagnosis, but since the book does not purport to be a clinical neurology this does not imply adverse criticism. This volume is an excellent introduction for serious students who plan to become neurologists but it is too detailed for the average medical student. Neurologists should have this work on their shelves for rapid reference concerning problems in localization requiring anatomic data and for periodic reviews of applied anatomy. There can be no simplified or philosophic preface to nervous diseases; the only adequate preface is a thorough grounding in structure and function which this book adequately presents.

**Der Rheumatismus: Sammlung von Einzeldarstellungen aus dem Gesamtgebiet der Rheumaerkrankungen.** Herausgegeben von Professor Dr. Rudolf Jürgens, Stellv. Direktor der Universitätsklinik für natürliche Heil- und Lebensweisen und Chefarzt des Augusta-Hospitals, Berlin. Band VIII: Behandlung rheumatischer Erkrankungen mit Ultra-Kurzwellen. Von Professor Dr. Erwin Schleich, leitendem Arzt der Balserischen Stiftung Glessen. Boards. Price, 7 marks. Pp. 105, with 27 illustrations. Dresden & Leipzig: Theodor Steinkopff, 1938.

This is the eighth of a series of monographs on rheumatism, the entire series being edited by Prof. Rudolf Jürgens. It is aimed at clarifying the indications for ultra short wave therapy in the rheumatic diseases and at pointing out that there is much more to this method of therapy than the mere technical aspects. The author ably reviews the indications for ultra short wave therapy and the technics that should be employed. As he himself says however this is not a subject which can be gained from books, and actual practice is as necessary as it is in surgery.

**A Challenge to Sex Censors.** By Theodore Schroeder. Privately printed to promote the aims of the Free Speech League. Boards. Pp. 159, with portrait. New York City, 1938.

This privately printed brochure is such an incoherent fanatical argument for free expression of sexual material that it deserves no serious review in a medical journal. The author has spent his life writing for free speech; his bibliography dates back thirty years, so that it seems he continues from force of habit.

**Essai de traitement de la migraine et de l'épilepsie par les solutions hypertoniques: Etude clinique et expérimentale.** Par le Docteur Jean-François Buvat, interne des hôpitaux psychiatriques de la Seine. Papier. Pp. 156. Paris: Librairie E. Le François, 1938.

From reading the first part of this work, one may deduce that the author, more in desperation than anything else, treated a patient who had severe migraine and epileptic equivalents with a 20 per cent solution of sodium chloride and bromide and observed considerable relief in symptoms. Thereupon he applied this method of treatment to thirty-five epileptic and seven migrainous patients, experimenting a little with different methods of administration and also with magnesium sulfate. Finally he seems to have hunted around for a possible explanation of the effects observed. He found this medication (sodium chloride 2 Gm., sodium bromide 2 Gm., sterile distilled water 20 cc.) most effective in cases of status. By practicing the injections three times a week he was able to

reduce the frequency of both the epileptic and the migrainous attacks. The author's principal experimental work was the observation of the fall in cerebrospinal fluid pressure following the intravenous injections of the hypertonic solution, averaging about 35 per cent within an hour. Further experiments on epileptic and nonepileptic subjects showed usually a moderate rise both in red blood corpuscles and in leukocytes, and an increased rapidity of the absorption of water given by intracutaneous injection. The majority of this Paris thesis, however, is taken up with a rather ill digested review of the opinions of others on the subject of epilepsy and migraine (the bibliography covers twelve pages) and with the inevitable case reports.

## Bureau of Legal Medicine and Legislation

### MEDICOLEGAL ABSTRACTS

**Medical Practice Acts: Defrauding Federal Government as Crime Involving Moral Turpitude.**—The appellant physician pleaded guilty in a federal court to certain counts in an indictment which charged that while he was a medical examiner for the United States Veterans' Bureau he presented for approval and payment false and fraudulent accounts with the intent to cheat and defraud the United States. He was sentenced to imprisonment. Later, the Department of Law Enforcement of Idaho, a state in which he was licensed to practice medicine, after notice and hearing revoked his license, in accordance with section 53-2107, Idaho Code Annotated (a section of the Idaho medical practice act), which authorizes the revocation or suspension of the license of a person convicted of a felony in a state or federal court, or convicted of any crime involving moral turpitude. The district court, Ada County, Idaho, affirmed the order of the department and the physician appealed to the Supreme Court of Idaho.

The physician contended that the department abused its discretion in revoking instead of suspending his license. He argued that in order to revoke a license it is incumbent on the state to show conclusively that the licensee is not fit to be entrusted with the powers and duties of a practitioner of medicine and that he had been convicted of nothing the doing of which disqualified him from the proper practice of his profession. To construe the Idaho medical practice act, the physician urged, to mean that a license can be revoked because its possessor has been convicted of a crime the commission of which does not involve moral turpitude would render the medical practice act unconstitutional. But, said the Supreme Court, the crimes to which he pleaded guilty did involve moral turpitude. They were acts of dishonesty and, although a dishonest man may be skilled in the practice of medicine, to allow him to practice that honored profession would bring disgrace on it and would expose the public to the misconduct of the criminally inclined. It is well within the police power of the state to prevent this. The court thought that the conduct of the physician was such as clearly justified the department in revoking his license rather than in suspending it. The order of the department revoking his license to practice was accordingly affirmed.—*Craft v. Balderston, Com'r of Law Enforcement (Idaho), 78 P. (2d) 122.*

**Medical Practice Acts: Electrocoagulation of Tonsils by Chiropractor; Use of Anesthetics.**—Joyner, a chiropractor, was convicted of practicing medicine without a license and appealed to the Supreme Court of Mississippi.

Chiropractic, said the court, is generally defined to be a philosophy, science and art dealing with the adjustment of the articulations of the spinal column by hand for the removal of the cause of disease and other bodily ailments. Joyner had no license to practice medicine but was licensed, the court said, to practice chiropractic.<sup>1</sup> According to the evidence introduced

by the state, Joyner, for a fee, attempted to remove the tonsils of a patient by electrocoagulation, after having "treated the cavity of his mouth with a liquid which had the effect of benumbing or deadening the walls of the mouth and his tongue." The chiropractor did not deny that he used a needle in treating the tonsils and that he applied the electric treatment. He did deny, however, that the liquid he used was a medicine or anesthetic, claiming that it was "Nature's Aid" and bore a label that it was a natural nonpoisonous germicidal antiseptic good for indigestion, ptomaine poisoning, cuts, etc. The conflict in the evidence, the court said, as to whether the liquid used was a medicine, anesthetic, or mineral water was resolved by the jury against Joyner. The "probability or improbability," the court continued, "of undertaking to insert a needle in a tonsil sore enough to contain a pus formation and apply an electric current thereto without using an anesthetic was peculiarly a question for the jury." While the liquid was not suggested, recommended or prescribed for the cure of the diseased tonsils, it was used for the palliation of the ailment during the process of its treatment. Its use, therefore, clearly constituted the practice of medicine within the following definition of that term as contained in the medical practice act:

"The practice of medicine shall mean to suggest, recommend, prescribe, or direct for the use of any person, any drug, medicine, appliance, or other agency, whether material or not material, for the cure, relief, or palliation of any ailment or disease of the mind or body, . . . after having received, or with the intent of receiving therefor . . . any . . . compensation." *Code of 1930, Sec. 1099, as amended.*

The treatment of disease by the use of surgical instruments and other appliances, the court continued, the use of medicine and drugs, and treatment by means of electricity, known as electrotherapy, are methods commonly adopted by physicians and surgeons. A physician is defined in the standard dictionaries as a person legally qualified and engaged in the general practice of medicine "as distinguished from one likewise skilled in the art of healing who specializes in surgery." Electrotherapy is the "use of different forms of electric machines for therapeutic purposes." Since the use of electrical appliances for the treatment of disease is ordinarily regarded as pertaining to the field of medicine or surgery, a person may not lawfully engage in such practice without being licensed as a physician and surgeon. Joyner, having no license authorizing him to practice medicine and surgery, was without authority to attempt to remove tonsils by electrocoagulation.

The trial court did not err, said the Supreme Court, in excluding evidence offered by Joyner to show that the National School of Chiropractic, which he attended, taught as a part of the course of study the use of the methods adopted by him in treating the patient in question. The sole issue on the trial was whether the treatment administered constituted the practice of medicine and surgery as defined in the medical practice act and in the decisions of the courts.

The judgment of conviction was therefore affirmed.—*Joyner v. State (Miss.), 179 So. 573.*

## Society Proceedings

### COMING MEETINGS

- American Academy of Orthopedic Surgeons, Memphis, Tenn., Jan. 15-19.
- Dr. Carl E. Badgley, 1313 East Ann St., Ann Arbor, Mich., Secretary.
- American Orthopsychiatric Association, New York, Feb. 23-25. Dr. Norvelle C. La Mar, 149 East 73d St., New York, Secretary.
- Annual Congress on Industrial Health, Chicago, Jan. 9-10. Dr. C. M. Peterson, 535 North Dearborn St., Chicago, Secretary.
- Annual Congress on Medical Education and Licensure, Chicago, Feb. 13-14. Dr. W. D. Cutter, 535 North Dearborn St., Chicago, Secretary.
- Eastern Section, American Laryngological, Rhinological and Otolological Society, Boston, Jan. 11. Dr. Frank E. Kittredge, Masonic Temple, Nashua, N. H., Chairman.
- Middle Section, American Laryngological, Rhinological and Otolological Society, Sioux City, Iowa, Jan. 19-20. T. R. Gittins, Davidson Bldg., Sioux City, Iowa, Chairman.
- Society of Surgeons of New Jersey, Newark, Jan. 28. Dr. Walter B. Mount, 21 Plymouth St., Montclair, Secretary.
- Southern Section, American Laryngological, Rhinological and Otolological Society, New Orleans, Jan. 14. Dr. Francis E. LeJeune, Maison Blanche, New Orleans, Chairman.
- Western Section, American Laryngological, Rhinological and Otolological Society, Spokane, Wash., Jan. 29. Dr. Frederic G. Sprowl, Medical Arts Bldg., Spokane, Wash., Chairman.

1. The laws of Mississippi do not provide for the issuance of licenses to practice chiropractic. The state licensing agency, the state board of health, advises that the court was evidently misled by the record and that, in fact, Joyner had no license authorizing him to practice chiropractic in Mississippi.

## Current Medical Literature

### AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1928 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (\*) are abstracted below.

#### Alabama State Medical Assn. Journal, Montgomery

S: 165-196 (Nov.) 1938

- The Anemias: Their Diagnosis and Treatment with Report of Cases. E. D. Lineberry, Birmingham.—p. 165.  
Chronic Varicose Ulcers: Treatment in General Practice. G. R. Smith, Ozark.—p. 169.  
Postoperative Treatment of Laparotomies. C. L. Rutherford, Mobile.—p. 170.  
Ocular Manifestations of Sinus Disease. E. R. Nodine, Andalusia.—p. 172.  
Measles. J. J. Repa, Montgomery.—p. 175.

#### American Journal of Cancer, New York

34: 169-332 (Oct.) 1938

- Monocytic Leukemia and Other Neoplastic Diseases Occurring in Mice Following Intrasplenic Injection of 1:2-Benzpyrene. J. Furth and O. B. Furth, with assistance of C. Breedis, New York.—p. 169.  
Occurrence of Cancer in Rats Treated with Estrone. C. S. McEuen, Montreal.—p. 184.  
Action of Colchicine on Transplanted Malignant Lymphoid Neoplasm in Mice of the C3H Strain. F. J. Lits, A. Kirschbaum and L. C. Strong, New Haven, Conn.—p. 196.  
Lipomatosis of Central Nervous System. A. B. Baker and J. M. Adams, Minneapolis.—p. 214.  
Hodgkin's Disease with Ulcerative Involvement of Skin. S. B. Pessin and E. A. Pohle, Madison, Wis.—p. 220.  
\*Fatal Case of Deep-Seated Epidermoid Carcinoma of the Breast with Widespread Metastasis. N. C. Foot and S. W. Moore, New York.—p. 226.  
Angiomatosis Cerebri: Case. J. Zeldenrust, Leiden, Netherlands.—p. 234.  
Leukemic Lymphoblastoma in a Calf: Hematologic and Histologic Study. J. Stasney and W. H. Feldman, Rochester, Minn.—p. 240.  
A Sex Difference in Incidence of Bone Tumors in Mice. F. C. Pybus and E. W. Miller, Newcastle-on-Tyne, England.—p. 248.  
Multiple Neoplasms in Sarcoma Strain of Mice. F. C. Pybus and E. W. Miller, Newcastle-on-Tyne, England.—p. 252.  
Progressive Growth Stages of a Heritable Melanotic Neoplastic Disease in Fishes from the Day of Birth. M. Gordon and G. M. Smith, New Haven, Conn.—p. 255.

#### Epidermoid Carcinoma of Breast with Metastasis.—

Only one case of a deeply seated epidermoid carcinoma of the breast was encountered by Foot and Moore in a series of 200 mammary carcinomas from a group of 331 breast tumors collected from 11,599 surgical specimens over a period of five years. The 0.5 per cent occurrence is misleading, as the case is the first of the sort seen by the senior author in twenty-five years. From the observations in this case the authors conclude that it is an example of metaplastic transformation of duct into covering epithelium, followed by a process of metastasis in which the emigrating cells retained and passed on the new characteristics acquired during the course of metaplasia. A lump had been present at the site for twenty years. Presumably this represented an area of fibrocystic disease which underwent the Schimmelbusch type of development and, later becoming malignant, went over to carcinoma, showing metaplasia. Although a radical mastectomy was performed, three months later the mass again became painful and, although the axillary nodes had been examined carefully and found free from metastases, the tumor recurred in the arm and was growing extensively in the lungs and possibly elsewhere two months after operation. The patient died four months after the mastectomy. All the metastases adhered to the spinocellular type of epidermoid carcinoma. There was no indication of an origin other than in the lining of glandular ducts.

#### American Journal of Diseases of Children, Chicago

56: 957-1188 (Nov.) 1938

- Osteochondritis Ischiopubica in Childhood. F. J. Corper, Chicago.—p. 957.  
Basal Energy Metabolism and Creatinine in the Urine: II. Prediction of Basal Heat Production from Creatinine. N. B. Talbot, Ann H. Stewart and Frances Broughton, Boston.—p. 965.  
\*Second Attacks of Poliomyelitis. J. A. Toomey, Cleveland.—p. 969.  
Iron Deficiency in Pregnant Rats: Its Effect on the Young. H. L. Alt, Chicago.—p. 975.  
Value of an Increased Supply of Vitamin B<sub>1</sub> and Iron in the Diet of Children: Paper III. Pearl Summerfeldt and J. R. Ross, Toronto.—p. 985.  
\*Cryptorchidism Treated with Gonadotropic Preparations: III. Surgical Repair of Cryptorchidism With and Without Gonadotropic Therapy. J. A. Bigler, Highland Park, Ill.; L. M. Hardy, Chicago, and H. V. Scott, Fort Wayne, Ind.—p. 989.  
Red Blood Cell Values in Adolescence. E. R. Murgage and Marjory I. Andresen, Denver.—p. 997.  
Vitamin C in Human Pregnancy and Lactation: I. Studies During Pregnancy. H. M. Teel, Bertha Sharpley Burke and Ruth Draper, Boston.—p. 1004.  
Id.: II. Studies During Lactation. T. H. Ingalls, Ruth Draper and H. M. Teel, Boston.—p. 1011.  
Osteopetrosis (Marble Bones). W. M. Clifton, Chicago; A. Frank, Malden, Mass., and S. Freeman, Chicago.—p. 1020.  
Microsedimentation of Erythrocytes in Infants and in Children. J. L. Rogatz, New York.—p. 1037.  
Tetany Syndrome in Newborn Infants: Remote Deposit of Calcium Salts Following Injection of Calcium Gluconate. W. R. Shannon, St. Paul.—p. 1046.  
Feeding the Infant with Cleft Palate with the Aid of a Dental Plate: Report of Five Cases. J. H. Sillman, New York.—p. 1055.  
\*Treatment of Peritoneal Syndrome and Erysipelas-like Lesions of Skin in Nephrosis. C. A. Aldrich, Winnetka, Ill., and H. H. Boyle, Chicago.—p. 1059.  
Adrenal Neuroblastoma: Report of Case and Review of Literature. J. L. Redman, H. A. Agerty, O. F. Barthmaier and H. R. Fisher, Philadelphia.—p. 1097.
- Second Attacks of Poliomyelitis.**—Toomey records the eighteenth case of a second attack of poliomyelitis. The case described was similar to the cases reported by others but the author does not feel that this case was an instance of a bona fide second attack of poliomyelitis. He postulates his objections on the theory that a person who has had poliomyelitis is a prey not so much to another attack of the same disease as to other diseases, such as influenza, measles and scarlet fever, which involve the few remaining peripheral nerve fibers and their cells of origin. He believes that the subsequent paralyses in his case were the result of influenza affecting the few remaining nerves and cells. It could have been toxic neuronitis in a person who had an old poliomyelitis. In the presence of any acute infection, such as influenza, bronchopneumonia, measles, coryza due to the virus of the common cold or scarlet fever, or in the presence of an injury, one has a right to question the diagnosis of a second attack of poliomyelitis and to insist that first toxic neuronitis be ruled out. If acute infections do aggravate the clinical condition of an old poliomyelitis, as has been shown experimentally, few of the reported cases in the literature can qualify as actual instances of a second attack of poliomyelitis.

**Cryptorchidism and Gonadotropic Preparations.**—For comparison, Bigler and his colleagues treated seventy-two patients having eighty-five instances of cryptorchidism either with surgical intervention alone or with gonadotropic therapy and operation. Forty-three patients were subjected to operation alone. Seven had operations and some time later were given a gonadotropic substance, and twenty-two were first treated with a gonadotropic principle and then operated on because of failure of the testes to descend completely. Slightly better results were obtained when a gonadotropic substance was given before operation than when operation alone was resorted to. The age of the patient and the position of the testes are probably not the only determining factors among the causes of atrophic undescended testes. Postoperative treatment with a gonadotropic principle had no beneficial effects on the testes which had been operated on, either in preventing or in correcting atrophy. The best results seemed to occur between the ages of 7 and 10 years with all forms of treatment. The gonadotropic principle should be given a fair trial in the



treatment of cryptorchidism in boys more than 7 years of age. If complete recovery does not occur after adequate therapy, operation should be considered.

**Treatment of Peritoneal Syndrome in Nephrosis.**—Aldrich and Boyle discuss the peritoneal syndrome and the cutaneous erysipelas-like lesions complicating nephrosis. The cutaneous lesions occurred on the lower part of the trunk, the lower extremities and the genitalia but never higher. The peritoneal syndrome was observed in practically all of the twenty-two children who had erysipelas-like lesions of the skin. Recently the authors frequently observed asthmatic bronchitis in children with nephrosis. Human erysipelas convalescent serum was instituted as routine treatment when the peritoneal syndrome appeared with or without cutaneous lesions. At first erysipelas serum was used but later convalescent scarlet fever serum was used instead. In all cases in which it was possible to use a vein the serum was given intravenously. No untoward reactions were noted. The amount used was from 60 to 100 cc. The immediate mortality from the peritoneal syndrome complicating nephrosis has been decidedly reduced; only five fatalities occurred in twenty-two attacks. Among previous patients afflicted with the disease who were not so treated, two of three children died. The reasons why patients presumed to have a pneumococcal infection should respond favorably to convalescent serum from patients with streptococcal infections are that convalescent serums have long been known to have non-specific beneficial effects on patients with various diseases and it is possible that the intravenous injection of this amount of normal serum may influence the nephrotic element favorably and thus put the patient in better condition to fight the peritoneal or the cutaneous infection. All patients with the erysipelas-like lesions promptly recovered after the serum treatment whether or not the peritoneal syndrome was present. This fact may be of some importance in making a prognosis when both complications occur. The most serious prognosis is encountered in those cases in which the patients have definite septicemia.

### American Journal of Physiology, Baltimore

124: 279-568 (Nov.) 1938. Partial Index

- Relationship of Kidney Function to Glucose Utilization of Extra-Abdominal Tissues. H. Bergman and D. R. Drury, Los Angeles.—p. 279.  
Experimental Analysis of Human Locomotion. A. W. Hubbard and R. H. Stetson, Oberlin, Ohio.—p. 300.  
Response of Smooth Muscle of Gallbladder at Various Intravesical Pressures to Cholecystokinin. H. Doubilet, New York, and A. C. Ivy, Chicago.—p. 379.  
Effect of Ether Anesthesia on Volume of Plasma and Extracellular Fluid. F. F. McAllister, Baltimore.—p. 391.  
Immediate Effects of Occlusion of Coronary Veins on Collateral Blood Flow in Coronary Arteries. D. E. Gregg and D. Dewald, Cleveland.—p. 435.  
\*Respiratory and Circulatory Adjustments to Erect Posture. F. A. Hitchcock and J. K. W. Ferguson, Columbus, Ohio.—p. 457.  
Adaptive Value of Absorption of Fats into Lymphatics. V. Johnson and W. Freeman, Chicago.—p. 466.  
Extrinsic and Intrinsic Pathways Concerned with Intestinal Inhibition During Intestinal Distention. W. B. Youmans, W. J. Meek and R. C. Herrin, Madison, Wis.—p. 470.  
Electrocardiographic Changes and Concentration of Potassium in Serum Following Intravenous Injection of Potassium Chloride. A. W. Winkler, H. E. Hoff and P. K. Smith, New Haven, Conn.—p. 478.  
Analysis of Factors Involved in Varying Effects of Carbon Dioxide on Respiratory Rate. S. Sobin and H. C. Nicholson, Ann Arbor, Mich.—p. 491.  
Studies on Physiologic Effects of Leukotaxine. V. Menkin and M. A. Kadish, Boston.—p. 524.  
Mechanism of Regulation of Blood Sugar by the Liver. S. Soskin, Chicago; H. E. Essex, J. F. Herrick and F. C. Mann, Rochester, Minn.—p. 558.

**Respiratory and Circulatory Adjustments to Erect Posture.**—Further investigation as to the cause of the decrease in the carbon dioxide content of the alveolar air on assuming the erect posture has been carried out by Hitchcock and Ferguson. They find that on the assumption of the erect posture there occur (1) a marked drop in the alveolar carbon dioxide, (2) the accumulation of an oxygen debt and the retention of carbon dioxide, (3) a decrease in the carbon dioxide content of venous blood in the upper limbs and an increase in the carbon dioxide content of venous blood in the lower limbs, and (4) an increase in the volume of the functional residual air. These changes are independent of alterations in pulmonary ventilation, which increases in some subjects and decreases in others. The theory is advanced that the primary cause of the lowered alveo-

lar carbon dioxide is simple dilution resulting from the increased volume of functional residual air and that once established this lower level of alveolar carbon dioxide is maintained by an impairment of carbon dioxide transport from the dependent parts of the body and presumably an increased circulation rate in the arms and thorax. This results in the lower alveolar carbon dioxide being reflected in the venous blood of the arms. The results suggest that such changes as occur in pulmonary ventilation are the result of carotid sinus reflexes and decreased cerebral circulation and that it is unnecessary to postulate any proprioceptive stimuli to the respiratory center.

### American Journal of Surgery, New York

42: 287-480 (Nov.) 1938

- Sarcoma of the Uterus. J. Kotz and M. S. Kaufman, Washington, D. C.—p. 289.  
A Simple, More Complete Obstetric Chart. H. S. Fist, Los Angeles.—p. 294.  
Complications of the Weak Foot (Subtalar Dystrochoides). J. Graham, Springfield, Ill.—p. 299.  
\*Muscular Rheumatism and Spina Bifida Occulta. R. J. Dittrich, Fort Scott, Kan.—p. 318.  
Analysis of Standard Methods of Treating Fracture of Femur: Based on Analysis of 100 Consecutive Cases. D. M. Vickers, Cambridge, N. Y.—p. 332.  
Infection and Gangrene of Extremities in the Diabetic: Diagnosis and Treatment. M. Grodinsky, Omaha.—p. 339.  
Hypervitamin Therapy in Surgical Practice. M. G. Vorhaus, New York.—p. 350.  
\*Pectenosis and Pectenotomy in Pruritus Ani: Preliminary Report. M. G. Spiesman, Chicago.—p. 356.  
\*Misgivings on Mineral Oil as a Laxative. J. W. Morgan, San Francisco.—p. 360.  
Mandelic Acid: Its Therapeutic Value and Limitations. G. Carroll, B. Lewis and L. Kappel, St. Louis.—p. 365.  
Observation on Sulfanilamide in Urology. F. A. Reuter, Washington, D. C.—p. 368.  
Nephropostis. J. P. Robertson and P. L. Singer, Birmingham, Ala.—p. 379.  
Surgical Indications in Thyroid Disorders. B. A. Goodman, New York.—p. 387.  
Ingrown Toenail: Operation by Electrosurgery. S. Vernon, Willimantic, Conn.—p. 396.  
Chronic Appendicitis: Appendectomy in Absence of History of Acute Appendicitis or of Appendical Colic. M. Kraemer, Newark, N. J.—p. 398.

**Muscular Rheumatism and Spina Bifida Occulta.**—Dittrich presents a study of ten cases of muscular rheumatism. This is a disability characterized by pain and tenderness of skeletal muscle and excessive fatigue of muscles on physical exertion. Regularly associated with such disorders are defects of the sacral spine, which are interpreted as spina bifida occulta. Combined with the osseous malformation are deposits of abnormal tissue within the spinal canal. These consist of (1) fibrous cords between the ventral aspects of the laminae and the nerve roots in the canal and (2) masses of fibro-adipose tissue surrounding the nerve roots. These abnormal structures are considered adequate to upset the function of the nerves. Surgical removal of the abnormalities results in relief of symptoms.

**Pectenosis and Pectenotomy in Anal Pruritus.**—Spiesman states that the mahogany fibers of the sphincter muscles are below the pecten band. The pecten fibers are white. He found pecten bands in nearly all cases presenting abnormal anal tightness. Since Abel had suggested pectenotomy for pruritus ani, the author has performed 250 pectenotomies (forty-eight for intractable anal pruritus). Pectenotomy was performed on all patients with anal tightness who did not respond to the usual pruritus treatment within a period of three weeks. The increased blood supply to the anal canal following the operation results in an absorption of fibrous connective tissue of the pecten band, similar to the absorption of fibrous connective tissue around a healed varicose ulcer, preventing reunion of the pecten band. Of the forty-eight cases reported, relief was not obtained in two. After a period of five years of trial, pectenotomy in the author's experience is one of the noteworthy advances in proctologic surgery for the relief of common anorectal conditions including intractable anal pruritus.

**Liquid Petrolatum as Laxative.**—Morgan lists the disturbing normal physiologic processes and pathologic changes which may attend the use of liquid petrolatum as an intestinal lubricant: 1. Liquid petrolatum lubricates the rectosigmoid and makes a reservoir of the rectum. 2. It makes complete evacuation impossible. 3. It has a deleterious effect on the

nutritional economy of fat soluble vitamins. 4. It hastens the motility of the intestinal contents and thereby prevents complete digestion. 5. It may interfere with the process of intestinal absorption. 6. Liquid petrolatum interferes with the healing of postoperative wounds in the anorectal region and may induce hemorrhage. 7. It is often the indirect cause of anal pruritus. 8. Evidence is accumulating that liquid petrolatum may be absorbed, producing pathologic changes in the liver and other abdominal viscera.

### Archives of Neurology and Psychiatry, Chicago.

40: 857-1066 (Nov.) 1938

- Tentorial Pressure Cone. G. Jefferson, Manchester, England.—p. 857.  
Physicochemical Properties of Brain, Especially in Senile Dementia and Cerebral Edema: Differential Ratio of Skull Capacity to Volume, Specific Weight, Water Content, Water-Binding Capacity and  $\mu$  of the Brain. L. Alexander and J. M. Looney, Worcester, Mass.—p. 877.  
\*Mentality of Dispensary Epileptic Patients. Margaret R. Barnes and J. L. Fetterman, Cleveland.—p. 903.  
Studies in Diseases of Muscle: VI. Progressive Peroneal Muscular Atrophy: Report on a Family, with Study of Heredity and of Metabolism of Creatine and Creatinine. S. M. Small and A. T. Milhorat, New York.—p. 911.  
Electro-Encephalogram in Bromide Intoxication. M. A. Rubin and L. H. Cohen, Worcester, Mass.—p. 922.  
\*Late Damage from Roentgen Irradiation of the Human Brain. W. Scholz, Munich, Germany, and Y. K. Hsü, Peiping, China.—p. 928.  
The Medulloblast and the Medulloblastoma: Study of Human Embryos. J. Kershman, Montreal.—p. 937.  
\*Myoclonic Epilepsy. R. R. Grinker, H. Serota and S. I. Stein, Chicago.—p. 968.  
Experimental Study of Macular Representation in the Monkey. G. L. Maisson, St. Louis; P. Settlage, Chicago, and W. F. Grether, New Haven, Conn.—p. 981.  
Anoxia and Neural Metabolism. R. W. Gerard, Chicago.—p. 985.  
Meningioma of the Lateral Ventricle: Report of Two Cases. J. G. Lyster, Jacksonville, Fla.—p. 997.  
Ependymal Cyst of Cervicodorsal Region of the Spinal Cord. I. Hyman, W. B. Hamby and S. Sanes, Buffalo.—p. 1005.  
Pituitary Cachexia (Simmonds' Disease): Report of Case with Autopsy. D. E. Plummer and J. R. Jaeger, Denver.—p. 1013.  
Familial Occurrence of Tic Douloureux. W. Allan, Charlotte, N. C.—p. 1019.

**Mentality of Epileptic Patients.**—Barnes and Fetterman determined the mentality of thirty-five epileptic patients by using the Stanford revision of the Binet test for general intelligence. Each of these patients was tested from three to eight times at intervals of a year or more. Temporary fluctuations were elicited, but on the average there was no steady deterioration. Only one patient presented regular losses. Some patients receiving treatment showed gains. The more critical Babcock test revealed a loss of efficiency amounting to one year. This amount does not represent pathologic deterioration, but it is a loss of mental efficiency of statistical significance. For patients who show deterioration, the basic disease responsible for the epilepsy rather than the conspicuous convulsion is the determining factor. The authors believe that the personality problems of an epileptic person are often due to the social and psychologic reactions to his disease rather than to any change in intelligence. This may be lessened by provision for training and sheltered workshops.

**Cerebral Damage from Irradiation.**—According to Scholz and Hsü, two deteriorated young patients with schizophrenia whose heads had been irradiated with 4 erythema skin doses through six portals in three days died about one and a half years after exposure without showing any definite focal neurologic symptoms. However, at necropsy the brains showed severe damage, which could be referred to disturbances in circulation of the blood. They consisted of (1) numerous and more or less extensive foci of necrosis of tissue, (2) peculiar changes, seen in other irradiated brains, in the form of severe fibrosis of vessels and deposition of peculiar homogeneous substances in the walls of the vessels and in the surrounding nerve tissue, and (3) changes in the walls of the vessels consisting of impregnation of the elastic layer with a dustlike fatty material and development of foam cells in the intima, and even in the lumen, which had a certain similarity to the process of hyalinization and which may perhaps be considered as a disturbance in the function of the vessel as a barrier due to the effect of irradiation.

**Myoclonic Epilepsy.**—Grinker and his associates discuss the history of a family in which there were two living persons with myoclonic epilepsy and several epileptic persons in the

same and previous generations. This family was studied clinically and with the encephalographic technic, by means of which the position of myoclonic epilepsy in the group of convulsive states is hypothesized. There were, besides the patients, an epileptic, homicidal paternal grandmother, a depressed, suicidal father, a myoclonic, deteriorated aunt, and two siblings suffering from convulsions complicating other diseases. The histories of the two myoclonic patients were typical. The disease began with convulsions, followed by myoclonia, intellectual deterioration and cerebellar symptoms. The pathologic changes seen in the specimen taken for biopsy were those of a chronic degenerative process in the parenchyma, with no amyloid bodies. The authors suggest that myoclonia is a homologue of continuous or intermittent prodromes sometimes evident, but often obscured, in other types of epilepsy. A feeling of malaise, irritability, depression, and the like, is masked clinically, whereas myoclonia is obvious. Electro-encephalographic tracings of prodromes in the psychic sphere may show evidences of a "building-up" process similar to that in the myoclonic prodromes. This, of necessity, would be convincing evidence that in other epilepsies as well the seizure is not a sudden catastrophe but an end result of a crescendo-like alteration in rhythm, perhaps self precipitating.

### Archives of Otolaryngology, Chicago

28: 663-840 (Nov.) 1938

- Diagnosis and Differential Diagnosis of Deafness. S. J. Crowe, Baltimore.—p. 663.  
Stapes, Fissula Ante Fenestram and Associated Structures in Man: I. From the Embryo of Seven Weeks to That of Twenty-One Weeks. B. J. Anson, J. E. Karabin and J. Martin, Chicago.—p. 676.  
Use of Sulfanilamide in Otolaryngology: Review of Literature. H. P. Schenck, Philadelphia.—p. 698.  
Morphologic and Roentgenologic Aspects of Temporal Bone: Study of 536 Bones, with Special Reference to Pneumatization. C. C. R. Jackson, Cleveland.—p. 748.  
Chronic Progressive Deafness, Including Otosclerosis and Diseases of the Inner Ear. G. E. Shambaugh Jr., Chicago.—p. 780.

### Journal of Clinical Investigation, New York.

17: 699-822 (Nov.) 1938

- \*Study of Some of the Physiologic Effects of Sulfanilamide: II. Methemoglobin Formation and Its Control. A. F. Hartmann, Anne M. Perley and H. L. Barnett, St. Louis.—p. 699.  
Plethysmographic Method for Quantitative Measurement of Blood Flow in the Foot. E. A. Stead Jr. and P. Kunkel, Boston.—p. 711.  
\*Blood Flow and Vasomotor Reactions in the Foot in Health, in Arteriosclerosis and in Thrombo-Angiitis Obliterans. P. Kunkel and E. A. Stead Jr., Boston.—p. 715.  
Insulin and Zinc Content of Normal and Diabetic Pancreas. D. A. Scott and A. M. Fisher, Toronto.—p. 725.  
Iodine Balance in Nodular Goiter. I. D. Puppel and G. M. Curtis, Columbus, Ohio.—p. 729.  
\*Use of Skin Test with Type Specific Polysaccharides in Control of Serum Dosage in Pneumococcal Pneumonia. C. M. MacLeod, C. L. Hoagland and P. B. Beeson, New York.—p. 739.  
Response of Diabetics to a Standard Test Dose of Insulin. G. Klatskin, Rochester, N. Y.—p. 745.  
Distribution of Ascorbic Acid Between Cells and Serum in Relation to Its Urinary Excretion. M. Heinemann, New Haven, Conn.—p. 751.  
Excretion of Porphyrins in Congenital Porphyrria. K. Dobriner, New York; W. H. Strain, H. Guild, Baltimore, and S. A. Localio, New York.—p. 761.  
Mechanism of Excretion of Vitamin C by the Human Kidney. Elaine P. Ralli, G. J. Friedman and S. H. Rubin, New York.—p. 765.  
Studies in Temperature Sensation: IV. Stimulation of Cold Sensation by Radiation. J. D. Hardy and T. W. Oppel, New York.—p. 771.  
Coagulation Defect in Hemophilia: Studies on Refractory Phase Following Repeated Injections of Globulin Substance Derived from Normal Human Plasma in Hemophilia. F. J. Pohle and F. H. L. Taylor, Boston.—p. 779.  
Direct Method for Estimation of Skin Distensibility with Its Application to Study of Vascular States. W. A. Sodeman and G. E. Burch, New Orleans.—p. 785.  
Carbohydrate Tolerance After Protamine Insulin: Its Bearing on Physiology of Insulin Secretion. H. T. Ricketts, Chicago.—p. 795.

**Methemoglobin Formation and Sulfanilamide.**—Hartmann and his co-workers studied the factors leading to the accumulation and disappearance of methemoglobin in patients to whom sulfanilamide was administered and they reach the following conclusions: 1. Reasonably close agreement exists between the direct spectroscopic determination of methemoglobin and the determination of non-oxygen carrying hemoglobin. 2. In the majority of patients receiving 0.1 Gm. or more of sulfanilamide per kilogram of weight every twenty-four hours cyanosis develops and so far methemoglobin has been observed in every case of cyanosis. 3. There is marked

individual variation in both the rate at which and the degree to which methemoglobin accumulates, although the dosage of sulfanilamide, its concentration in the blood and perhaps the extensiveness of the infection seem to have a direct relationship. 4. Methylene blue causes rapid disappearance of cyanosis with simultaneous reduction in the concentration of methemoglobin, when given intravenously in single doses of from 1 to 2 mg. per kilogram or when given orally in doses of from 1 to 2 grains (65 to 130 mg.) repeated every four hours. The latter method also prevents any appreciable formation of methemoglobin if started simultaneously with the administration of sulfanilamide.

**Blood Flow in Foot and Vascular Diseases.**—Kunkel and Stead determined the blood flow in the foot in health, in arteriosclerosis and in thrombo-angiitis obliterans under standard conditions by the plethysmographic method. The flow was recorded as cubic centimeters of blood per minute per hundred cubic centimeters of tissue. The blood flow to the foot reached a constant level after thirty minutes at 43 C. The flow at this temperature has been designated as the "maximal" flow. The average maximal blood flow to the foot in normal persons was 17.1 cc., with the highest 25.9 and the lowest 11.1 cc. The maximal blood flow in the foot showed no appreciable decrease with age (17 to 67 years) in the presence of a normal cardiovascular system. The average maximal blood flow in the hand, when calculated in relation to the cutaneous area, was 30 per cent greater than that in the foot. The vasomotor reactions of the hand and foot were qualitatively similar. A deep inspiration, however, induced constriction of vasomotor origin in both the hand and the foot. In arteriosclerosis and thrombo-angiitis obliterans the maximal blood flow to the foot was reduced 50 per cent without symptoms or trophic disturbances. When the flow was reduced to one-third the normal value or below, symptoms or trophic disturbances usually occurred. In both arteriosclerosis and thrombo-angiitis obliterans severe intermittent claudication in the calf was in some cases incapacitating, though the blood flow in the foot was as great as in many normal persons. Thus the presence of an adequate supply of blood to the foot did not eliminate the possibility of obliterative disease involving the vessels of the calf.

**Cutaneous Test with Polysaccharides in Pneumonia.**—In controlling the dosage of immune serum in the treatment of pneumonia resulting from pneumococcus types I, II, III, V, VII and VIII, MacLeod and his associates used the cutaneous test with the homologous specific polysaccharide. The test was valuable and entirely satisfactory in determining when a sufficient amount of serum had been given in 77 per cent of the 104 cases. At the appearance of a positive reaction no further serum was given, and the subsequent course of events justified the reliance placed on the test. Antiserums prepared in the horse and the rabbit have been used in treatment, and the cutaneous test has been found equally applicable in the control of dosage of the two kinds of immune serum. Thirteen patients showed a positive cutaneous test before the administration of specific antiserum and at a time when the disease was advancing. In four of these cases the circulating antibody was determined before serum was given and in no instance were agglutinins demonstrable. The occurrence of positive reactions under these conditions makes it imperative to perform the test on each patient before serum therapy is begun, since, without knowing the initial reactivity of the skin, one may be entirely misled by the results of subsequent tests. The cutaneous test can be used as a guide to serum dosage only in those patients who show a negative reaction before type specific antibody has been given. Except in one allergic person who had extensive eczema, the positive cutaneous reactions in the thirteen patients cannot be explained. These "falsely positive" reactions occurred with preparations of type I and II polysaccharide which were known to be protein free and which did not contain any demonstrable "C substance." However, the test substances may have contained small amounts of other extraneous materials which could produce nonspecific reactions in the skin of certain individuals. When a "falsely positive" reaction occurred with the homologous polysaccharide, similar reactions were generally observed with preparations of other type specific polysaccharides in the same person.

## Michigan State Medical Society Journal, Lansing

37: 957-1052 (Nov.) 1938

- Public Health, the Product of Individual Preventive Medicine. H. Emerson, New York.—p. 973.  
Use of Crystalline Insulin in Treatment of Patients with Severe Diabetes. S. S. Altshuler and R. Leiser, Detroit.—p. 980.  
Amautotic Family Idiocy (Tay-Sachs Disease). D. B. Davis, Grand Rapids.—p. 983.  
Electroencephalography: Introduction and Present Status. A. J. Derbyshire and S. S. Bohn, Detroit.—p. 985.  
Newer Studies and Experiences with Latex Protective Rubber Surgical Dressing. D. H. O'Donnell, Detroit.—p. 991.  
Ten Years of Treatment and Progress in Case of Chronic Myeloid Leukemia: Lipid Distribution in Leukocytes and Erythrocytes. M. W. Poole, Betty N. Erickson, H. H. Williams, Detroit; H. J. Burkholder, Alpena, and T. Leucutia, Detroit.—p. 993.  
Evaluation of Urinary Shreds in Prenuptial Examinations. G. Schinagel, Detroit.—p. 999.

## Pennsylvania Medical Journal, Harrisburg

42: 97-208 (Nov.) 1938

- Surgery of the Colon. H. B. Stone, Baltimore.—p. 105.  
Diagnostic Problems in Surgical Kidney Disease. M. Muschat, Philadelphia.—p. 111.  
\*Exophthalmic Goiter in Patients Past Age Fifty: Comments Based on Series of 322 Cases. I. Bram, Philadelphia.—p. 117.  
Bleeding Peptic Ulcer. D. B. Pfeiffer and A. G. Martin, Philadelphia.—p. 121.  
Diagnosis and Surgical Treatment of Rectal Diseases. J. M. Deaver, Philadelphia.—p. 125.  
Functions of the Peritoneum: Their Effect on Surgical Pathology of Peritonitis. J. W. Kennedy, Philadelphia.—p. 130.  
Respiratory Tract Allergy in General Practice. R. A. Kern, Philadelphia.—p. 133.  
Importance of Periodic Health Examinations Relative to Heart Disease. E. B. Rentschler, Reading.—p. 139.  
Preoperative and Postoperative Management of Surgical Gallbladder Patient: Further Effort to Reduce Operative Mortality and Post-operative Morbidity. B. B. V. Lyon, Philadelphia.—p. 142.

**Exophthalmic Goiter in Advanced Years.**—While in his experience the sex incidence of exophthalmic goiter in children is approximately one male to twenty females and in young adults one male to five females, in his series of 322 patients between the ages of 50 and 78 years Bram found the incidence to be approximately one male to two females. Tachycardia in the average case was moderate. Most patients presented a more or less chronic syndrome of several years' duration, commonly with such dominating circulatory symptoms as arterial hypertension, auricular fibrillation, precordial distress, shortness of breath and impending or actual congestive cardiac failure. Other noteworthy clinical characteristics of exophthalmic goiter in this series were that the thyroid was only moderately enlarged, occasionally it was quite normal in size, exophthalmos was of slight or moderate degree and frequently associated with conjunctival congestion and swelling of the eyelids, the tremor was constant and coarser than in young patients, and loss in weight, fatigability and weakness were characteristically marked. The basal metabolic rate was generally moderately elevated and occasionally quite normal despite otherwise typical signs and symptoms of exophthalmic goiter. Therefore the test was of little assistance in the diagnosis in this series but when taken repeatedly served to indicate progress of treatment. In differential diagnosis neurocirculatory asthenia and primary circulatory conditions including malignant hypertension and Parkinson's syndrome must be excluded. Because of inadequate circulatory reserve and advancing years these patients are poor surgical risks and treatment should more often be conservative.

## Texas State Journal of Medicine, Fort Worth

34: 455-516 (Nov.) 1938

- The General and Specific Treatment of Pneumonia. J. A. Kolmer, Philadelphia.—p. 460.  
Serum Therapy in Pneumonia. J. S. Sweeney, Dallas.—p. 464.  
Treatment of Carcinoma of the Fundus of the Uterus. O. T. Woods, Dallas.—p. 469.  
Advances in Treatment of Carcinoma of Cervix. C. L. Martin, Dallas.—p. 471.  
Urinary Tract Complications from Carcinoma of Cervix. A. I. Folsom and H. A. O'Brien, Dallas.—p. 476.  
Cholelithiasis. J. T. Krueger, Lubbock.—p. 480.  
Rational Management of Hemorrhoids. C. Rosser, Dallas.—p. 484.  
A Psychologic Approach to the Insomnia Problem. H. R. Gold, Dallas.—p. 488.  
Organic Factors in Personality Disorders: Problems in Diagnosis and Treatment. J. M. Hill, Houston.—p. 492.  
The Forward March of Radiology. R. T. Wilson, Austin.—p. 496.

## FOREIGN

An asterisk (\*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

**Bristol Medico-Chirurgical Journal**

55: 151-210 (Autumn) 1938

- Some Problems in the Diagnosis and Treatment of Intracranial Tumors. F. W. Willway.—p. 151.  
Some Tuberculous Conditions. H. Chitty.—p. 161.  
The Vitamin B Complex. H. M. Sinclair.—p. 173.  
Medicinal Waters at Burnham-on-Sea. J. A. Nixon.—p. 191.

**British Journal of Rheumatism, London**

1: 73-148 (Oct.) 1938

- Investigations in Rheumatic Cases. J. W. Shackle.—p. 75.  
Pathologic Anatomy of Rheumatic Fever. D. H. Collins.—p. 88.  
\*Surgical Method of Relief for Intractable Pain in Osteo-Arthritis of the Knee. A. E. M. Woolf.—p. 97.  
Subcutaneous Nodules. C. O. Hawthorne.—p. 109.  
Electrical Treatment in Rheumatic Conditions. L. D. Bailey.—p. 117.  
The Heberdens. W. Hale-White.—p. 129.  
Indications for the Employment of Brine Baths in Treatment of Chronic Rheumatic Diseases. A. R. Neligan.—p. 137.

**Relief of Intractable Pain in Osteo-Arthritis.**—Woolf describes a method of relieving the intractable pain of osteo-arthritis of the knee joint. The method consists in the injection into the affected knee joint of the patient's own fat which has been liquefied and converted into oil. No relief is to be expected in the true rheumatoid cases. When the soft periarticular tissues are affected—especially if the process is marked in the fingers—fat injection is unlikely to relieve pain. As a consequence the author has reserved the method for cases of osteo-arthritis, more especially of the dry type, with grating on movement of the affected joints; the knee is the easiest to inject and the most responsive. The method should be used only in intractable cases in which the pain is not relieved by other known methods of treatment. The author has usually obtained the fat from the abdominal wall below the umbilicus or in a thin person from the outer upper part of the thigh. A transverse incision is made and, after the skin has been undermined, a mass of fat is excised. By the adoption of an elliptic incision with a piece of skin, less undercutting is necessary and hematomas have been entirely avoided. The fat is shaken in saline solution to wash off the blood. It is then placed in a porcelain dish and cooked over an electric flat cooker or hot plate. As soon as the fat begins to cook, it is essential to keep on cutting it. If this is not done the connective tissue envelops round the fat droplets coagulate, which prevents the oil from escaping and the result is a charred mass. As the fat is cooking and cut up oil is seen to exude and this is drained into another dish and filtered through sterile gauze. In from eight to ten minutes the mass of fat is converted into oil, and all that remains in the original heated dish is a small charred mass. When the oil is cooled to 120 F. it is injected. A wide-bore needle is used and 30 cc. is injected under the patella, 15 cc. on each side. The bone must not be touched. As soon as the injection is made, the joint is vigorously moved and massaged. Of the thirty injections made in twenty-four cases sixteen were successful, seven were failures, three were doubtful and in four the immediate result was good but they were not followed up.

**British Medical Journal, London**

2: 929-976 (Nov. 5) 1938

- Some Nutritional Problems of Childhood. L. G. Parsons.—p. 929.  
A System of Radium Dosage. H. S. Souttar.—p. 933.  
Antipernicious Principle: Some Experiments with Urine. E. Jéquier and G. R. M. Apsey.—p. 934.  
Early Diagnosis of Schizophrenia. W. Mayer-Gross.—p. 936.  
\*Incidence of Pathogenic Staphylococci in the Nose. A. M. McFarlan.—p. 939.  
\*Sulfanilamide in Treatment of Acute Mastoiditis. V. G. Horan and S. G. French.—p. 942.

**Pathogenic Staphylococci in the Nose.**—In order to determine the incidence of pathogenic staphylococci in the apparently healthy nose, McFarlan examined the nasal swabs from 101 undergraduates, thirty-three children and thirty-one adults. None of these subjects had or had recently had a staphylococcal or nasopharyngeal infection. In most cases the

growths from the two nostrils were similar. In fifteen cases the growth from one side was heavier or contained more *Staphylococcus aureus* and less *Staphylococcus albus* colonies than the other; but such differences were slight and the results are given as positive or negative for each individual. Staphylococci were present in thirty-one of the adults, twenty-four children and ninety-one students. Pathogenic staphylococci were present in the nose of twenty of twenty-nine patients with staphylococcal infections. In nine undergraduates who had had a series of boils a year or more before the investigation there were seven who had hemolytic staphylococci in the nose. This shows that the local condition does not necessarily recur when pathogenic staphylococci are present in the nose. The growths of staphylococci obtained from the nose of some patients with staphylococcal infections were pure *Staphylococcus aureus* and more profuse than usual, but similar growths were obtained occasionally from healthy persons. It is possible that pathogenic staphylococci may be transferred by the patient's fingers from the nose to a lesion elsewhere. Since pathogenic staphylococci are so often present in an apparently healthy nose it is reasonable to take all possible precautions to prevent reinfection from that source. The frequency with which pathogenic staphylococci occur in the nose of healthy persons makes it possible that their presence in the nose of patients with staphylococcal infections in other parts of the body is merely a reflection of the carrier rate of the community in which they live. If the serologic types of staphylococci prove to be as stable and numerous as Griffith's streptococcal types it may be possible to obtain evidence in favor of the occurrence of reinfection from the nose by finding that the nasal strain is serologically identical with that isolated from the lesion elsewhere. At present the isolation of pathogenic staphylococci from the nose of a patient with a chronic staphylococcal infection cannot be considered as proof that reinfection is occurring.

**Sulfanilamide in Acute Mastoiditis.**—According to Horan and French, during the year following the routine use of sulfanilamide in otitis media the ratio of acute mastoiditis to acute otitis media has been greatly reduced, from 22.7 to 4.5 per cent. The percentages were obtained from the statistical returns of the Royal Naval Hospital, and the average for the years 1934, 1935, 1936 and the early half of 1937, when sulfanilamide was not being used, is compared with the year comprising the latter half of 1937 and the early half of 1938, when sulfanilamide was used in a routine way. From January 1934 to June 1937 the number of yearly deaths from the complications of acute suppurative otitis media averaged 2.85, while from June 1937 to June 1938 there were no deaths from this cause. The authors make no claims with regard to the efficacy of the drug in the treatment of otitis media, but the figures are consistent with the view that it is a preventive of the complications of this disease. It is not claimed that every case of otitis media was streptococcal in origin, for swabs were not taken in all of them. All those in which swabs were taken proved to be due to a hemolytic streptococcus, and during the past winter and spring there has been, in the district from which these cases came, almost a streptococcal epidemic, consisting of tonsillitis, scarlet fever (which has been severe), and the like. The sulfanilamide was used in a purely "shotgun" manner on admission. The results seem to justify its use, for, even if the otitis does not respond to the treatment and mastoiditis develops, no harm has been done and the patient's resistance is in no way impaired by the drug. In no case was the administration of sulfonamide prolonged for more than fourteen days. Chronic otitis media has not been considered in this group of patients, as the majority of them had no previous record of otitis media.

**Edinburgh Medical Journal**

45: 741-828 (Nov.) 1938

- Traumatic Meningeal Hemorrhage: Review of Seventy-One Cases. J. H. Pringle.—p. 741.  
Harvey in Scotland. H. Wade.—p. 761.  
Results of Recent Studies on Anterior Pituitary Hormones. J. B. Collip.—p. 782.  
Lister and His Contemporaries in Edinburgh. C. E. Douglas.—p. 805.  
Isolation of *Bacillus Tuberculosis* from Sputum: Comparison of Antiformin and Sulfuric Acid Methods. A. Saenz and J. T. Paterson.—p. 818.

**Journal of Laryngology and Otology, London**

53: 685-736 (Nov.) 1938

Contribution to Study of Middle Ear Suppuration, with Special Reference to Pathogeny and Treatment of Cholesteatoma. A. Tumarkin.—p. 685.

**Lancet, London**

2: 1041-1094 (Nov. 5) 1938

Pulmonary New Growths: Pathology, Diagnosis and Treatment. R. C. Brock.—p. 1041.

Granulocytopenia Following Administration of Sulfanilamide Compounds. F. D. Johnston.—p. 1044.

\*Bulgarian Treatment of Postencephalitic Parkinsonism: Comparison with English Belladonna. D. Hill.—p. 1048.

New Carbon Dioxide Absorber. F. T. Evans.—p. 1050.

Unusual Infections Following Cerebral Operations, with Description of Diplococcus Mucosus (von Lingelsheim). S. T. Cowan.—p. 1052.

Myeloid Leukemia Following Pernicious Anemia and Complicated by Tertiary Syphilis. H. H. F. Barns and M. L. Rosenheim.—p. 1054.

\*Procaine Injection Treatment of Herpes Zoster. S. Rosenak.—p. 1056.

**Treatment of Postencephalitic Parkinsonism.**—Hill treated fourteen patients suffering from postencephalitic parkinsonism with a decoction of Bulgarian belladonna. Improvement followed in ten patients who showed decreased rigidity; of these, four also showed diminished tremor. The oculogyric crises were not much improved. Ten patients also gained weight. When English belladonna decocted first in wine and later in acid alcohol was substituted, the improvement in the parkinsonism was maintained. The patients did not at first notice the substitution. On the acid alcohol decoction, signs of belladonna poisoning became pronounced in six patients; this may be because it contains more alkaloids of belladonna than the wine decoction. The therapeutic properties of Bulgarian belladonna do not seem to differ from those of its English equivalent.

**Procaine Hydrochloride in Herpes Zoster.**—Rosenak injected each intervertebral ganglion and the prevertebral sympathetic cord of twenty-two patients suffering from herpes zoster with 8 cc. of a 0.5 per cent solution of procaine hydrochloride. In the two patients with trigeminal zoster the gasserian ganglion was infiltrated, but this time only 1 and 2 cc. respectively of the same solution was used following Härtel's technic. The treatment should be abandoned if the only way of reaching the ganglion is through an area of infected vesicles. About fifteen minutes after injection, full segmentary anesthesia results. Zoster of the thorax, neck and extremities should be treated in this way only when accompanied by particularly severe pain, for the method is not harmless. Except in two cases the pain ceased and the vesicles dried within twenty-four to forty-eight hours.

**Medical Journal of Australia, Sydney**

2: 671-716 (Oct. 22) 1938

Mental Disorder and Childbirth. J. McGeorge.—p. 671.

Mental and Nervous Diseases Associated with Childbirth. H. B. Williams.—p. 677.

Arthritis Deformans from the Point of View of an Orthopedist. N. Little.—p. 681.

\*Investigation of Source of Staphylococcal Infection in Acute Osteomyelitis. S. Williams and Cecily Timmins.—p. 687.

Endonasal Antrostomy: X-Ray Study. T. G. Millar.—p. 689.

**Source of Staphylococci in Acute Osteomyelitis.**—Williams and Timmins point out that in the figures for the number of patients suffering from acute osteomyelitis treated at the Children's Hospital, Melbourne, there are yearly fluctuations which suggest that the relative frequency of the disease might in some way be influenced by differences in the types of staphylococci prevalent among the child community at different periods. Staphylococcus aureus is a not uncommon inhabitant of the upper part of the respiratory tract. If certain strains producing subclinical infections were more likely than others to settle in a damaged epiphyseal junction, a possible explanation of these periodic fluctuations would be available. A few children of a small series of cases, on staphylococcus cultures from the respiratory tract and the bony lesion, harbored the same staphylococcus at the two sites. The study indicates that in a large series of cases, adequately investigated, it would be possible in a certain proportion of cases to provide definite evidence of the port of entry of the staphylococcus responsible for the serious lesion. A method of differentiating staphylococcus strains by means of their susceptibility to lysis in broth by a series of bacteriophages is described.

**Practitioner, London**

141: 577-692 (Nov.) 1938

Earache. W. M. Mollison.—p. 577.

Affections of the External Ear. G. Scarff.—p. 586.

\*Chronic Running Ear in Childhood. J. Crooks.—p. 594.

The Intracranial Complications of Ear Disease. J. P. Stewart.—p. 603.

The Deaf Child. P. Franklin.—p. 613.

Recent Advances in Hearing Aids. Phyllis M. Tookey Kerridge.—p. 625.

Treatment by Manipulation. H. J. Burrows and W. D. Collart.—p. 633.

\*Pulp Infections of the Fingers. A. L. d'Abreu.—p. 648.

Clinical Application of Renal Efficiency Tests. J. V. Wilson.—p. 653.

Collection of Pathologic Specimens. A. Renshaw.—p. 665.

Diet in Health and Disease: XVII. Diet in Diabetes Mellitus. T. I. Bennett.—p. 677.

**Chronic Running Ear in Childhood.**—Crooks states that the starting point of otorrhea is acute otitis media, which results from infection of the upper part of the respiratory tract, often influenced by the presence of an infective focus in the nose or throat. The acutely inflamed ear must be treated assiduously and no focus of infection in the nose and throat must be overlooked. If discharge from the ear persists for a few weeks after acute otitis media there is great danger of its becoming chronic. The removal of adenoids or drainage of an infected sinus or of the mastoid cells may be imperative if otorrhea is to cease. Mastoid infection may supervene at any time during otorrhea. It may be the cause of the continuance of the discharge, and it can become a danger to the life as well as to the health of the patient. The discharging middle ear should be treated as such only after other sources of infection have been excluded.

**Pulp Infections of the Fingers.**—According to d'Abreu, absolute immobilization of the affected finger from the outset of infection should be provided by means of a short splint. If the infection has spread to a tendon sheath the patient is confined to bed. An incision is used only when suppuration is present and this is usually detected by tenderness, fluctuation and pyrexia. In suppuration of the finger, pulp fluctuation is a late sign. When the pulp of the finger loses its normal softness and feels hard, immediate operation is indicated. An excellent rule is that a sleepless night due to an infected finger means pus under tension, and incision is urgently needed. The incision recommended is a single lateral one for early cases and bilateral ones for patients seen later when the whole pulp is involved. Sometimes complete decompression of the space by a horseshoe flap extending round the tip of the finger is required. A tourniquet round the base of the finger is essential. The lateral incision is deep and is made from above downward, i. e. toward the tip of the finger. By this means there is no danger of continuing the incision too far beyond the base of the phalanx. The end of the incision toward the tip should be slightly curved. A small rubber drain is preferable to gauze packing and is always used when bilateral incisions are employed. For the after-treatment adequate splintage, elevation and heat are of great value. If the patient is at all ill systemically, rest in bed is of great value. Local rest is provided by splints. The other fingers should be free from bandages or splints and they should be exercised. The provision of heat and hot fomentations or by placing the hand under an electrically heated hand cradle is useful to relieve pain and to encourage hyperemia. Hot fomentations are abandoned as soon as the finger shows evidence of being sodden, for such swelling involves the lips of the wounds and hinders adequate drainage.

**Chinese Medical Journal, Peiping**

54: 301-396 (Oct.) 1938

Vitamin A Deficiency in Man: Resolution of Cutaneous Lesions Following Parenteral Administration of Carotene. C. N. Frazier and H. C. Li.—p. 301.

Paralysis of the Vocal Cords: Review of Thirty-Six Cases. J. Hua Liu and Y. H. Hsu.—p. 315.

Coarctation of the Aorta: Report of Case. J. S. McNair.—p. 331.

Survey of Intestinal Parasites in Chinese Hospital Patients in Shanghai. Mary N. Andrews.—p. 341.

Studies on Hunan Local Food Products: III. Vitamin C Content of "Vegetable Water." T. F. Su.—p. 351.

Innocuous Intravenous Infusion with an Appeal for Establishment of Central Solution Laboratories for Cholera Relief. H. Thomas and L. C. Ting.—p. 358.

**Annales de Dermatologie et de Syphiligraphie, Paris**

9: 849-928 (Oct.) 1938. Partial Index

- \*Urethral Localization of Venereal Lymphogranuloma. E. Bizzozero and A. Midana.—p. 849.  
Histogenesis of Mycosis Fungoides. F. Cailliau.—p. 857.

**Urethral Localization of Venereal Lymphogranuloma.**—Bizzozero and Midana review the literature on the urethral localization of venereal lymphogranuloma, calling attention to observations by Kleeberg, Frei, Wiese, Klestadt, Bezecny, Faulbusch and others. They stress especially the high incidence of positive Frei reactions that have been observed in cases of Waelsch's type of urethritis. They subjected the patients with Waelsch's type of urethritis to Frei tests and examined the urine, Littre's glands, Morgagni's lacuna, the prostate, the seminal vesicles and the inguinal lymph nodes. They reach the conclusion that the majority of patients with urethritis of Waelsch's type are of the nature of a venereal lymphogranuloma. They found this to be the case in fifteen of eighteen cases. In all these fifteen cases the diagnosis was based on Frei's reaction, which was always verified by several controls. The endoscopic examinations revealed that the urethral lesions of these patients had a certain predilection for the verumontanum and the posterior urethra. Three of the cases were excluded because, although they were like the others in symptomatology and evolution, repeated tests with the urethral secretion in patients with venereal lymphogranuloma remained without reaction. This proves that not all the cases of Waelsch's type of urethritis are of the nature of a venereal lymphogranuloma. Discussing the treatment the author says that in some cases he obtained rapid cure by irrigations with a 1:4,000 solution of silver nitrate, followed by instillation, while in another case this treatment produced no improvement whatever. In several other cases the intravenous administration of iodine preparations effected considerable improvements, while in others their effect was slight. Finally, the treatment by antimony preparations produced good and lasting results.

**Journal de Médecine de Lyon, Lyons**

19: 623-652 (Nov. 5) 1938

- \*Obstetric Traumatism in Newborn with Polyvisceral Sclerosis: Eight Cases. J. Voron, R. Noël and H. Pigeaud.—p. 623.  
New Knowledge Relating to Epidemiology and Prophylaxis of Undulant Fever. E. Ledoux.—p. 631.  
Early Pneumothorax. L. Croizier and Mlle. Clepacz.—p. 637.  
Practical Pulmonary Stratigraphy. C. Gaillard.—p. 643.

**Polyvisceral Sclerosis in Newborn and Obstetric Traumatism.**—Voron and his associates state that during the last decade they attempted to determine the importance of obstetric traumatism undergone by the newborn in the course of labor. Studying the intracranial hemorrhages in aborted fetuses and stillbirths, they were able to show that there exist intracranial hemorrhages in four or five month fetuses expelled in the intact ovum and that in numerous stillbirths after an intracranial hemorrhage it is possible to demonstrate by means of clinical, serologic and microscopic investigations the existence of a congenital disorder, which appears to be responsible for the observed hemorrhagic lesions. The authors describe observations on eight infants who died in the obstetric clinic in Lyons either in the course of labor or shortly after delivery. The clinical circumstances made it possible to relate the deaths of these infants to a traumatism in the course of labor. However, microscopic studies on the liver, the spleen and the lung revealed sclerotic lesions in these different parenchymas which indicate the existence of a congenital disease that had evolved in the course of intra-uterine life. The authors conclude that every time an infant dies during labor or shortly after delivery the different visceral organs should be subjected to microscopic examinations, because these studies are likely to demonstrate the real cause of death. The existence of sclerotic lesions, when the clinical and serologic examinations have been negative, tend to prove that the fetus in the course of its intra-uterine development is sensitive to morbid influences which are as yet not exactly identified. The authors think that among other causes maternal alcoholism may be of pathogenic importance. They say that their observations support the contention

that the part played by obstetric traumatism in the death of newborn infants is more apparent than real and that often, even when the traumatism does play a part, its action is a contributing one, that is, it simply precipitates the death of an infant who has been made susceptible by a congenital disease which has evolved in the course of intra-uterine life.

**Presse Médicale, Paris**

46: 1609-1624 (Nov. 2) 1938.

- Experimental Renal Enervation: Physiopathologic and Pharmacodynamic Considerations. M. Bariéty and D. Kohler.—p. 1609.  
\*Herpetic Encephalitis: Apoplectic Form, Convulsive and Hallucinatory Form; Contagion by Herpetic Virus. G. de Morsier.—p. 1611.

**Herpetic Encephalitis.**—In less than a year de Morsier observed three patients in whom grave cerebral disturbances coexisted with an eruption of labial herpes. The first two cases that are described show close resemblance. The disorder began abruptly; the temperature rose to 39 C. (102.2 F.); the patients fell into coma, which persisted for forty-eight hours and meningeal symptoms appeared. The first patient showed signs of agitation during the period of coma. In this patient, the herpes appeared after two days, whereas in the second it did not appear until the eighth day. Regarding the cerebrospinal fluid, the author says that in the first case there was no leukocytosis but a hyperalbuminosis; in the second case polymorphonuclears and a moderate hyperalbuminosis were detected. Examination of the blood disclosed in both patients a mild leukocytosis without noticeable modification of the leukocytic equilibrium. The evolution was similar in the two cases. Eleven days after the onset of the coma, both patients could be discharged as cured. In the third patient the evolution was analogous to that of the first two, but the symptomatology differed in that the cortical symptoms predominated. There were intermittent convulsions with an aura, complex forced movements (nutations) and visual and auditory hallucinations accompanied by a certain degree of amnesia. Severe labial herpes appeared on the fifth day. The examination of the cerebrospinal fluid disclosed no inflammatory reaction, but the examination of the blood revealed a leukocytosis. All the alarming cerebral symptoms disappeared in about three weeks. The nurse who attended this patient developed a typical herpetic keratitis one week after the appearance of the labial herpes. The ophthalmologic examination of the nurse disclosed delicate epithelial vesicles in the central region of the cornea of both eyes. Reviewing the literature on herpes accompanied by meningeal and encephalitic symptoms the author finds that the majority of patients present meningeal symptoms. He distinguishes three clinical forms of herpetic encephalitis: (1) the meningeal form, which so far has been observed most frequently, and which may be relapsing, (2) the convulsive form with paresthesias and vertigo and (3) the comatose form with sudden onset. In the last part of his discussion he reviews experimental studies on the relation between herpes and cerebral disturbances. It has been demonstrated that the liquid from herpetic vesicles of human subjects, when injected into the cornea of rabbits, produces a dendritic keratitis. This keratitis can be transmitted from one animal to another. Some of the rabbits in which keratitis has been produced by the inoculation of herpetic material develop encephalitis which may terminate in death. The cornea of rabbits inoculated previously with the virus of encephalitis is immune against the herpetic virus. Herpetic virus derived from the brain of a rabbit which has died as the result of experimental herpetic encephalitis and introduced into the spinal cavity of a patient with post-encephalitic parkinsonism (for therapeutic purposes) may provoke an encephalitis of two or three weeks' duration which is accompanied by a cutaneous herpetic eruption. These therapeutic attempts never resulted in death. The author says that the opinions are still divided about the problem of the identity of the virus of encephalitis and herpes. He thinks that there is probably a relation between the herpetic virus and the cerebral symptoms presented by his patients. The fact that the nurse developed herpetic keratitis indicates the virulence and recalls to the author several small epidemics of herpes, one of which presented meningitic aspects.



**Monatsschrift f. Geburtshilfe u. Gynäkologie, Basel**

108: 237-292 (Sept.) 1938

\*Potassium and Sodium Content of Serum in Preeclamptic Conditions and Its Modification by Insulin Hypoglycemia. F. Posatti and W. Beiglböck.—p. 237.

Thirst-Fever in the Newborn. W. Hagedorn.—p. 247.

Casusistic Contribution to Life-Saving Action of Venesection in Pulmonary Edema That Developed After Operation for Tubal Rupture. H. Dörr.—p. 253.

Experimental Transplantation of Ovaries. Ziya Üstün.—p. 259.

Anemic Conditions in the Newborn. H. Lehndorff.—p. 264.

Intra-Abdominal Rupture Hemorrhages Caused by Anomalies of Placentation. G. Gaetgens.—p. 277.

**Potassium and Sodium in Preeclamptic States: Modification by Insulin.**—Posatti and Beiglböck, after showing that capillary spasm, a tendency to edema and an increase in blood pressure are the pathogenic factors of eclampsia, give special attention to the changes in the mineral content of the serum and tissues. They direct attention to the electrostatic theory of R. Keller, according to which the parenchymal cell on the one hand and the serum and the connective tissue on the other contain electrical charges, the serum and the connective tissue acting as the negative pole, the cell as the positive pole. Moreover, the ions in the biologic milieu are subject to electrical forces; some behave like bodies with a negative charge and wander to the positive pole, others like bodies with a positive charge and wander to the negative pole. The biologic substances can be differentiated into positive and negative ones. The positive ones include sodium, the negative ones potassium. The wandering of ions has been designated as "directed permeability." It becomes impaired under pathologic conditions, particularly when the capillary wall has been damaged by toxic influences. If this is the case, ions belonging to the serum enter the cell. Tissue analyses reveal a relative increase in the sodium content and a relative decrease in the potassium content. Of course, the other ions show a similar behavior, but sodium and potassium are selected as representatives of the antagonistic groups. The authors think that a change in the ion content of the tissues is one of the chief factors in all forms of serous inflammation; that is, in all conditions in which the capillaries become excessively permeable. In view of the shifting in the mineral content during pregnancy and especially during eclampsia, it may be assumed that here analogous factors are involved. Studies conducted by one of the authors (Beiglböck) revealed that during hypoglycemia induced by insulin the permeability changed in the opposite direction to that which is observed in "serous inflammations" and so it was decided to try insulin in the treatment of women with preeclamptic conditions. The authors give short case histories of six pregnant women and list in a table the effects of the insulin on the sodium and potassium contents. This table reveals that soon after the appearance of the hypoglycemic symptoms there takes place a noticeable decrease in the potassium content of the serum and a slight increase in the sodium content. The authors show that these changes induced by insulin are in the same general direction as those produced by the customary therapeutic measures: for instance, treatment of edema by restriction of the hydropigenous sodium and, on the other hand, the administration of large amounts of potassium. The question arises whether insulin could be used as an addition to the other therapeutic measures, but the authors are as yet unable to give a definite answer to this question.

**Annali Italiani di Chirurgia, Bologna**

17: 667-826 (Aug.-Sept.) 1938. Partial Index

\*Metabolism of Chlorides in Gastroduodenal Ulcer. G. Conti and G. Montanari.—p. 667.

Cholesterol in Experimental Acute Peritonitis. P. Baiocchi.—p. 691.

Experimental Discontinuous Interruption of Venous and Arterial Circulation of Kidney. P. Bassi.—p. 721.

Traumatic Rupture of Thoracic Duct. L. Giornelli.—p. 775.

**Chlorides in Gastroduodenal Ulcer.**—Conti and Montanari observed the action of the chlorides in the blood of twenty patients suffering from gastroduodenal ulcer who had to be operated on and also in five normal persons for control. The amount of chlorides in the blood and the chemistry of the gastric secretion were determined during fasting after preliminary removal of the gastric secretion followed by administration of an injection of 0.001 Gm. of histamine in solution.

The determinations were repeated at intervals of from fifteen to twenty minutes during the first four hours after the injection. The latter caused diminution of the chlorides in the blood, which was more intense and lasting in the patients than in normal persons, in emaciated and dehydrated patients than in those who were in regular nutritional condition. According to the authors the behavior of the curve of chlorides after the histamine injections depends on the fact that the metabolism of the chlorides in the organs and in the blood is disturbed. The power of the organs for storing chlorides is diminished and as a rule there is hypochloremia during fasting. Consequently neither the organs nor the blood can provide for the needs of chlorides in the increased process of gastric secretion. The authors point out the importance of the disturbance and advise preparing the patients by rechloridation with the administration of liberal amounts of sodium chloride in the food as well as by intravenous injections.

**Archiv für Kreislaufforschung, Dresden**

3: 125-224 (Nov.) 1938

\*Is Primary Hypertension in the Lesser Circulation Possible? Problem of Primary Pulmonary Sclerosis. M. Staemmler.—p. 125.

Investigations on Influence of Diphtheria on Size of Heart and on Tissue Changes in Myocardium. W. Masshoff.—p. 142.

Acute Intoxication with Digitalis in Man. K. Blumberger and C. Krüskemper.—p. 168.

Einthoven's Triangular Form of Electrocardiogram in Comparison with Other Forms of Leads. H. E. Hollmann and W. Hollmann.—p. 191.

Changes in ST and T Wave of Electrocardiogram in Course of Day ("Diurnal Fluctuations"). G. Hermann.—p. 209.

Experimental Alteration in Quantity of Blood: Behavior of Blood Pressure and Pulse Frequency After Withdrawal of Blood. H. Brünner and W. Mertens.—p. 223.

**Hypertension in Lesser Circulation.**—The question of the possibility of a primary hypertension in the lesser circulation arose in connection with hypertrophies of the right side of the heart which could not be explained by pulmonary disorders that are otherwise held responsible for them, and in which defects of the left side of the heart were absent. Staemmler calls attention to the fact that Wiese described in 1936 an apparently new type of arterial disease in the lesser circulation to which the term thrombendarteritis obliterans was applied. Hoenig described additional cases of this type during the following year, and Staemmler also observed a case. The disorder begins with a proliferation and detachment of the endothelium of the medium and small arterial branches and the formation of fibrinoid thrombi. The thrombi become organized, interspersed with blood vessels and connective tissue and are thus transformed first into vascularized granulation tissue and later into connective tissue, which narrows or completely obliterates the arterial lumen. This particular form of thrombendarteritis obliterans doubtless stands apart from the majority of the reported cases of so-called primary pulmonary sclerosis, although some of these cases show considerable resemblance to this form. The cause has received no attention as yet and so the author studies this problem in two cases. He arrives at the conclusion that a primary hypertension in the lesser circulation must be regarded as the cause of this form of thrombendarteritis obliterans. Reviewing the literature on this problem, he finds that Steinberg in 1929 regarded a hypertension in the lung as the primary factor that secondarily leads to "pulmonary sclerosis." As even more significant than this report by Steinberg the author considers one by Rosenthal in 1930. In the further discussion he points out that, if a primary hypertension in the pulmonary circulation by spastic contraction of the arterioles is regarded as the origin of this process, the many different anatomic aspects that are encountered in the same disease may be interpreted as manifestations of the different phases of the same process. The first stage is characterized by continuous contraction of the arterioles, hypertrophy of the musculature and increased resistance in the lesser circulation. The heart becomes adapted by means of hypertrophy. Greater demands on the walls of the arteries which, although not contracted themselves, are connected with spastic vessels results in an increase in the elasticity of all layers of the wall. During the second stage there exists excessive extension with impairment of the elastic fibers; reparative (compensatory) connective tissue prolifera-

tion in media and intima; impairment of the newly formed intima tissue, and fatty degeneration of the character of arteriosclerosis. During the third stage there exist, among other changes, necrosis of the musculature, inflammatory reactions, aneurysms, arteritis and so on. The fourth stage is characterized by the formation of thrombi, endothelial proliferation, organization, and obliteration of the arteries: the picture of thrombendarteritis pulmonalis obliterans. During the fifth stage the periphery of the lesser circulation becomes more confined, the hypertension is organically fixed, this reacts on the branches, there is pulmonary sclerosis, the right cardiac ventricle becomes dilated, there is a tendency to pulmonary infarcts, and so on. The author says that of course not every case passes always through all these stages. The aspects are variable because they depend on many different factors, for instance on the adaptability of the heart, the resistance of the vascular walls, the age of the patient and others.

### Klinische Wochenschrift, Berlin

17: 1529-1568 (Oct. 29) 1938. Partial Index

- Investigations on Influence of Riboflavin (Vitamin B<sub>2</sub>) and of Corticosterone on Experimental Renal Diabetes. F. Hoff.—p. 1535.  
Serology of Tuberculosis. F. H. Koss.—p. 1537.  
New Method for Testing Resistance of Small Cutaneous Vessels. G. Sack.—p. 1539.  
Quantitative Investigations on Action of Short Waves on Living Tissue (Wavelength 3.5 Meters). E. Hasché.—p. 1542.  
\*Action of Calcium on Basal Metabolism of Human Subjects. L. Goreczky and G. von Ludány.—p. 1544.  
Occurrence of Metachromatic Substance in Growing Tissue and Its Significance. B. Sylvén.—p. 1545.  
Action of Apoptropine in Human Subjects and Its Use in Treatment of Chronic Encephalitis. F. Duensing.—p. 1550.

**Action of Calcium on Basal Metabolism.**—Goreczky and von Ludány first review earlier investigations in which it was demonstrated that the administration of parathyroid extract to rats resulted first in a reduction and then in a 15 per cent increase in the oxygen consumption. It was found that this action of parathyroid extract on the basal metabolism can be explained by its effect on the calcium content of the serum. The initial reduction in the basal metabolism was accompanied by an increase in the calcium content of the serum. The same effects were noted when calcium was given to the rats by subcutaneous administration. These observations clearly indicate that there is an antagonism between the calcium content of the blood and the basal metabolism. The authors decided to repeat these experiments in human subjects. The tests were made on persons of both sexes and of various ages who were free from serious organic or functional disorders. It was found that an intravenous injection of calcium causes in human subjects a temporary decrease in the oxygen consumption but that after from one to three hours normal values are reached again. The so-called second phase (increase in the oxygen consumption), which was observed in animals after the administration of parathyroid extract or the injection of calcium, was observed in only two of the ten human subjects. During this second phase a compensatory hypocalcemia was observed. These tests clearly show that there is a close relationship between the calcium content of the blood and the basal metabolism.

### Strahlentherapie, Berlin

63: 225-400 (Oct. 28) 1938. Partial Index

- Attitude of Surgery to Irradiation Therapy of Malignant Tumors. F. Sauerbruch.—p. 256.  
Attitude of Radiology to Operation of Tumors. H. R. Schinz.—p. 268.  
Technic and Method of Irradiation of Esophageal Carcinoma. A. Adam.—p. 316.  
\*Roentgen Therapy of Chronic Tonsillitis. P. Hess.—p. 393.  
Roentgen Therapy of Sinusitis. L. Popp.—p. 399.

**Roentgen Therapy of Chronic Tonsillitis.**—Hess describes his experiences with roentgen irradiation of tonsillitis in 124 cases, of which 101 could be examined later. The technic of irradiation was the same for all groups in which the author classifies his material. The rays were applied with 180 kilovolts; the filter consisted of copper and aluminum, the distance was 30 cm. and the tonsillar fields were 6 by 8 cm. The tonsils were irradiated with 165 roentgens each. The two irradiations were given on successive days. To apply the rays to both sides in one day is not advisable because the roentgen treatment is followed by a swelling of the irradiated side of the neck, which

however subsides in twenty-four hours. The author says that the first group of patients, namely those with relapsing tonsillitis but without hyperplasia or complications, responded favorably to roentgen therapy; the treatment failed in only 10 per cent of these cases. In the second group, those with involvement of the regional lymph nodes, cure was obtained in all cases. Of the third group, those with hyperplasia and crypt formation, 20 per cent were refractory to the irradiation. In these cases the cure of the relapsing tonsillitis is independent of the involution of the hyperplasia. Roentgen therapy does not act satisfactorily on the hyperplasia of the tonsils. However, irradiation and surgery do not exclude each other but can be combined with good success. The author recommends irradiation as highly effective also in the treatment of carriers of diphtheria bacilli.

### Zeitschrift für Orthopädie, Stuttgart

68: 369-504 (Nov. 1) 1938. Partial Index

- Experiences with Stiffening of Arthrotic Flatfoot, of Pes Adductus and of Pes Equinovarus Paralyticus. E. Spira.—p. 369.  
Deformities of Extremities and Their Therapy. K. Daubenspeck.—p. 375.  
\*Investigations on Symptomatology and Etiology of So-Called "Coxa Vara Congenita" or "Coxa Vara Infantum." M. Zimmermann.—p. 389.  
Inhibition of Flexion in Knee Joint Caused by Old Injury of Internal Lateral Ligament (Tibial Collateral Ligament). W. Baumgartner.—p. 415.  
Congenital Dislocation of Shoulder. R. Pfeiffer.—p. 418.  
Multiple Congenital Rigidity of Joints. L. Horeysek.—p. 424.  
Noteworthy Observations in Congenital Bilateral Absence of Patella. G. Hohmann.—p. 460.

**Coxa Vara Congenita.**—Zimmermann discusses observations of sixty-five children (thirty boys and thirty-five girls) with "coxa vara congenita," seen at the orthopedic clinic in Munich during the years from 1924 to 1937. The ages of the patients ranged up to 18 years. The right hip was most frequently involved. The previous histories showed great similarity. The parents noted a slow onset of limping, combined with a waddling walk, fatigability and occasionally slight pains. None of the children showed other deformities, in addition to the coxa vara, and there were no indications of a connection between coxa vara congenita and congenital dislocation of the hip joint. Investigations of the family histories did not reveal hereditary transmission. The authors describe the clinical histories of two early cases of coxa vara congenita, concerning children of 14 and of 19 months. These two cases are compared to one described by Kreuz. With advancing age and load there is a progressive sliding off of the head of the femur into the lower portions of the acetabulum, a shifting of the epiphysal line from the horizontal to the vertical direction, and a triangular splitting up with atrophy on the inferior point of the neck of the femur. These changes are regarded as secondary signs of the deformity, for they are not present in the beginning. Inspection of the roentgenograms likewise disclosed no relations between coxa vara congenita and congenital dislocation of the hip joint. The roentgenograms never disclosed acetabular conditions like those that are observed in congenital dislocation of the hip joint. Discussing the etiology, the author assumes with Kreuz that congenital, endochondral ossification disturbances most likely play a part. The early recognizable collum varum, the greater distance between the ossific nucleus of the head and the neck, compared to the normal side, suggest a congenital developmental inhibition. The retarded appearance of the nucleus of the trochanter major as well as the belated closure of the synchondrosis ischiopubica on the diseased side give further support to this opinion. They should not be regarded as bridging symptoms to congenital dislocation of the hip joint. In view of the fact that Perthes' disease developed on the other hip in three cases of coxa vara congenita, the author considers a connection with this disease possible. The severity of the coxa vara is conditioned by time, that is, it increases with age, and by the extent of the ossification disturbances. The author reports three cases of coxa vara in which spontaneous cure resulted from early closure of the epiphysis and points out that closure of the epiphysis in this form is observed also after the subtrochanteric osteotomy. Discussing the treatment of early cases, he says that although the subtrochanteric osteotomy in its various forms is generally regarded as the method of choice, at his clinic an attempt is made with nonsurgical treatment.

**Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam**

82: 4953-5096 (Oct. 8) 1938. Partial Index

Sarcoma and So-Called Sarcoma of Mammary Gland. L. D. Eerland.—p. 4954.

\*Some Remarks on Perthes' Disease in Connection with Its Treatment. R. J. Harrenstein.—p. 4962.

Endemic Pellagra Cured by Nicotinic Acid. C. D. de Langen, J. C. Boswijk and C. L. C. van Nieuwenhuizen.—p. 4970.

Experimental Studies on Influence of Starvation on Consciousness: Importance for Psychiatric Expert. B. Stokvis and A. Naerebout.—p. 4977.

Simple Method to Obtain Good Microscopic Specimen of "Cobweb Clot" in Tuberculous Meningitis. H. K. G. Bartstra and M. A. Groenendal.—p. 4983.

Treatment of Meningitis by Sulfanilamide. J. E. Minkenhof.—p. 4986.

Treatment of Chorea Minor. S. Kroonenberg.—p. 4996.

**Perthes' Disease and Its Treatment.**—Harrenstein says that the cause of osteochondritis juvenilis coxae is as yet unknown. The author shows that in this condition there exists, besides destruction and necrosis in the head of the femur, also a productive process which becomes manifest in an enlargement of the proximal epiphysal disk of the femur. The roentgenogram of the diseased joint gives only incomplete information about the degenerative process in the bone and about the supporting power of the head of the femur, because decalcified areas on the roentgenogram can be simulated by various tissues. From initial stages of Perthes' disease, which in the roentgenogram appear identical, different forms develop apparently arbitrarily, now toward a nearly complete clinical recovery with reconstruction of the head of the femur, then again to a permanent gross deformity and defective function of the joint. An after-examination of fourteen patients who had been treated only by rest in bed and plaster cast, for the time that pain and stiffness of the joint made this treatment unavoidable, showed that in half of these cases ideal healing had taken place, with regard both to the form of the head of the femur and to the function of the joint. The therapeutic value of more radical methods of treatment therefore can be assessed only from the results obtained on large series of patients.

**Acta Medica Scandinavica, Stockholm**

96: 425-591 (Oct. 21) 1938

\*Influence of Vitamin A on External Secretion of Pancreas. K. Herfort.—p. 425.

Uric Acid in Blood and Urine in Bright's Disease. K. Brøchner-Mortensen.—p. 438.

\*Chronic Acetanilid Poisoning: Result of Continuous Use of Mixed Headache Powders or Similar Compounds. E. Lundsteen, E. Meulengracht and A. Rischel.—p. 462.

\*Parathyroids and Body Temperature. E. Ask-Upmark.—p. 481.

\*Treatment of Diseases of Joints with Progesterone. J. F. Touw and R. K. W. Kuipers.—p. 501.

Occurrence of Heterogenic Antibodies in Internal, Surgical and Cutaneous Tuberculosis and in Hodgkin's and Schaumann's Diseases. K. Hedén.—p. 509.

Experimental Contribution to Calcium Therapy of Allergic Conditions. P. Kallos and Liselotte Kallos-Deffner.—p. 519.

Transitory Lung Infiltrations with Eosinophilia. P. B. Gravesen.—p. 523.

Primary Complex in Infectious Diseases: Its Anatomic and Clinical Aspects. S. Gräff.—p. 571.

**Influence of Vitamin A on Secretion of Pancreas.**—A considerable subjective and objective alleviation of the symptoms of patients with anachlorhydria following treatment with vitamin A induced Herfort to examine the action of this vitamin on the external secretion of the pancreas because, although medication with vitamin A improved symptoms such as diarrhea, residues of poorly digested foods in the feces, poor appetite and emaciation, it did not influence the quantity of free hydrochloric acid. The author studied the action of vitamin A on the external secretion of the pancreas in thirty subjects, some of whom were healthy and some of whom had gastrointestinal disturbances. He observed that vitamin A exerts a considerable stimulating action on the external secretion of the pancreas whether it is given orally in the form of tablets or of an oil solution or whether it is administered by the parenteral route by intramuscular injection. He thinks that this excitation of the external pancreatic secretion explains the increase in appetite and weight which was noted in all subjects who received this

vitamin and that it is also the cause of the disappearance of the diarrhea and of the nondigested alimentary residues from the feces of patients with anachlorhydria. In a later report he intends to take up the question whether vitamin A acts on the external secretion of the pancreas by way of the nervous or of the humoral route, whether it exerts a stimulating effect also on the internal secretion of the pancreas and whether the effect exerted by vitamin A on the external pancreatic secretion will be of diagnostic value in disorders of this organ.

**Chronic Acetanilid Poisoning.**—Lundsteen and his associates give a historical review of the therapeutic use of acetanilid, of its chemistry, pharmacology and toxic effects, as well as of the already published cases of acute and chronic acetanilid poisoning. They report a number of personally observed cases of chronic acetanilid poisoning, the poisoning in these cases being due to continuous use of "mixed headache powders" or similar compounds. The reason these patients had started the use of the powders and tablets had been chronic headache. In the observed cases the most striking symptom was a peculiar cyanosis; the most disabling symptoms, however, were fatigue, headache, anemia and loss of weight. It is shown that the cyanosis is caused by the decomposition of acetanilid into dark colored derivatives of para-aminophenol and not due to methemoglobinemia, as is most commonly believed. The authors say that continuous use of acetanilid is followed by a peculiar and strong addiction. The substance has a transitory stimulating and elevating effect; continuous use, however, causes persistent fatigue and headache; that is, the symptoms that originally led to its use. Thus a vicious circle is being formed. It is emphasized that prescriptions for powders or tablets containing acetanilid ought to be nonrefillable.

**Parathyroids and Body Temperature.**—Ask-Upmark reviews, mainly from the clinical point of view, the present knowledge of the relation between the parathyroids and the body temperature. He describes four cases of hyperparathyroidism (osteitis fibrosa generalisata Engel-Recklinghausen) with especial regard to the behavior of the temperature. An elevation of the temperature above normal was observed in three of the four cases reported here. The nature of this increase in temperature is discussed. Since it may disappear with removal of the parathyroid adenoma, it is probably caused by the metabolic disturbances inherent in the disease. The temperature chart in hyperparathyroidism may present an undulation somewhat similar to the so-called Pel-Ebstein phenomenon. Rhythmic changes in temperature of this type may be caused by a pathologic sequence of events involving the reticulo-endothelial system and particularly the bone marrow. Occasionally the temperature in hyperparathyroidism may be subnormal. Attention is called to the seasonal character of the disorders of the parathyroids.

**Treatment of Articular Disorders with Progesterone.**—Touw and Kuipers treated three women who had articular disorders with injections of progesterone. The authors were induced to resort to this treatment by the observation that as soon as the patients became pregnant the articular disorders disappeared, to return again a few weeks after confinement. In the first patient it appeared that the complaints were caused by disturbances in the growth of the epiphyses of the hip joints with resulting arthrosis deformans, whereas the other two patients had chronic articular rheumatism (primary chronic polyarthrititis). The case histories indicate that the progesterone was administered by daily intramuscular injections of 2 cc. (10 units) during the second phase of the intermenstrual period. The results obtained with this treatment were favorable, but its mode of action is not understood as yet. The authors are as yet unable to estimate the duration of the improvement, but in one of the patients it has so far persisted for six months and in another for four months. In case of recurrence, the authors intend to apply the same treatment. However, they emphasize that the progesterone therapy is not necessarily indicated in all articular disturbances. They only wish to point out that there are patients in whom the anamnesis justifies treatment with progesterone.

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AMERICAN MEDICAL ASSOCIATION, CHICAGO, 1938

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- Acta Chirurgica Scandinavica. Stockholm.  
Acta Medica Scandinavica. Stockholm.  
Acta Obstetrica et Gynecologica Scandinavica. Stockholm.  
Acta Paediatrica. Stockholm.  
Acta Psychiatrica et Neurologica. Copenhagen.  
Acta Radiologica. Stockholm.  
American Heart Journal. St. Louis.  
American Journal of Cancer. New York.  
American Journal of Clinical Pathology. Baltimore.  
American Journal of Digestive Diseases. Huntington, Ind.  
\*American Journal of Diseases of Children. A. M. A., Chicago.  
American Journal of Hygiene. Baltimore.  
American Journal of Medical Jurisprudence. Boston.  
American Journal of the Medical Sciences. Philadelphia.  
American Journal of Obstetrics and Gynecology. St. Louis.  
American Journal of Ophthalmology. St. Louis.  
American Journal of Orthopsychiatry. Menasha, Wis.  
American Journal of Pathology. Boston.  
American Journal of Physiology. Baltimore.  
American Journal of Psychiatry. New York.  
American Journal of Public Health. New York.  
American Journal of Roentgenol. and Radium Therapy. Springfield, Ill.  
American Journal of Surgery. New York.  
American Journal of Syphilis, Gonorr. and Venereal Diseases. St. Louis.  
American Journal of Tropical Medicine. Baltimore.  
American Review of Tuberculosis. New York.  
Anales de la Facultad de Medicina de Montevideo.  
Anatomical Record. Philadelphia.  
Annaes Brasileiros de Gynecologia. Rio de Janeiro.  
Annales de Dermatologie et de Syphiligraphie. Paris.  
Annales de Médecine. Paris.  
Annali dell'Istituto "Carlo Forlanini." Rome.  
Annali Italiani di Chirurgia. Bologna.  
Annali di Ostetricia e Ginecologia. Milan.  
Annals of Internal Medicine. Lancaster, Pa.  
Annals of Medical History. New York.  
Annals of Otolaryngology and Rhinology and Laryngology. St. Louis.  
Annals of Surgery. Philadelphia.  
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Archivos Argentinos de Pediatría. Buenos Aires.  
Atti della Società Italiana di Ostetricia e Ginecologia. Rome.  
Australian Journal of Experimental Biology and Medical Science. Adelaide.  
Australian and New Zealand Journal of Surgery. Sydney.  
Beiträge zur klinischen Chirurgie. Berlin.  
Beiträge zur Klinik der Tuberkulose. Berlin.  
Bollettino. Milan.  
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Brain. London.  
Brasil-Médico. Rio de Janeiro.  
Bristol Medico-Chirurgical Journal.  
British Journal of Anaesthesia. Manchester.  
British Journal of Children's Diseases. London.  
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British Journal of Experimental Pathology. London.  
British Journal of Ophthalmology. London.  
British Journal of Physical Medicine. London.  
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British Journal of Rheumatism. London.  
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Bulletin of the Johns Hopkins Hospital. Baltimore.  
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Clinica Ostetrica. Rome.  
Clinical Science. London.  
Cuore e Circolazione. Rome.  
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 Zentralblatt für Chirurgie. Leipzig.  
 Zentralblatt für Gynäkologie. Leipzig.

## SUBJECT INDEX

This is an index to all the reading matter in THE JOURNAL. In the Current Medical Literature Department only the articles which have been abstracted are indexed.

The letters used to explain in which department the matter indexed appears are as follows: "BI," Bureau of Investigation; "E," Editorial; "C," Correspondence; "OS," Organization Section; "SS," Student Section; "ab," abstracts; the star (\*) indicates an original article in THE JOURNAL.

This is a subject index and one should, therefore, look for the subject word, with the following exceptions: "Book Notices," "Deaths," "Medicolegal Abstracts" and "Societies" are indexed under these titles at the end of the letters "B," "D," "M," and "S." State board examinations are entered under the general heading State Board Reports, and not under the names of the individual states. Matter pertaining to the Association is indexed under "American Medical Association." The name of the author, in brackets, follows the subject entry.

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